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No. XXV. OF VOL. I., 1927. LONDON, SATURDAY, JUNE 18, 1927 Pp. 128—Price 1s.
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An Address read before the Edinburgh Obstetrical Society on May 11th, 1927,

BY BECKWITH WHITEHOUSE, M.S. LOND., CH.M. BIRM., F.R.C.S. ENG.,

PROFESSOR OF OBSTETRICS AND DISEASES OF WOMEN, UNIVERSITY OF BIRMINGHAM; HONORARY GYNÆCOLOGICAL SURGEON, GENERAL HOSPITAL, BIRMINGHAM.

THERE is nothing, I think, more stimulating to research than to have work thoroughly discussed under the critical eye of friends. A worker in his own den, whether that den be the hospital ward or a pathological laboratory, is apt sooner or later to fall into a groove. Theory is liable to become an obsession, and without the therapeutic stimulus of free and open discussion, the result of research may be but an abortion—the unfinished and incomplete effigy of what might have been a real and beautiful entity. It is in this spirit, therefore, that I venture to submit certain observations on the menstrual function which have interested me during my work in the Midlands.

Now, the phenomena associated with the menstrual function may be studied in various ways. Briefly, these may be stated as follows:—

(*a*) By a comparison with the sexual phenomena noted in other species in the mammalian tree.

(*b*) By a study of material obtained at operation, at different periods in the sexual cycle, and especially during the actual menstrual function.

(*c*) By the investigation of the actual function, especially of the menstrual discharge, both in health and disease.

(*d*) By noting the effect both immediate and remote of excision of parts of the sexual apparatus at different periods of the sexual cycle.

(*e*) By the observation in animals and "homo" of the effect of injecting various tissue extracts.

These are the lines upon which we are working in Birmingham and which as time goes on have altered many of my preconceived ideas with regard to menstruation.

THE NATURE OF THE MENSTRUAL FUNCTION.

The first question that I propose to discuss is: "What is the menstrual function in the genus homo?" The generally accepted view, of course, is that it is a preparation of the uterus for the reception of the fertilised ovum. In other words, that it corresponds to the stage of pro-œstrum in the lower mammals. That this is not entirely correct I am firmly convinced from data which I shall shortly place before you. In order to make the position clear, however, it will be necessary to refer briefly to the phenomena associated with the sexual cycle in other mammalian types.

The period of the year when physiological activity of the reproductive system in mammals occurs has been called by Heape the "sexual season." At other times in the majority of wild species the reproductive organs are quiescent. During the sexual season, which, in the wild state, occurs usually but once a year, the female experiences a series of cyclical periods of sexual activity. Each of these successive periods during the sexual season constitutes an "œstrus cycle," divided by Heape into four subsections:—

(1) Anœstrum, or period of rest.

(2) Pro-œstrum, or period of endometrial growth and functional activity.

(3) Œstrum, or period of desire, when fertilisation is effected.

(4) Pregnancy, or "pseudo-pregnancy."

During the anœstrum or rest period the uterus is in a state of quiescence. Its glands are small and the organ is relatively anæmic. The ovaries, so far as the Graafian follicles are concerned, are also inactive. It is a period of slow growth and development of the follicles, which do not appear on the surface of the ovaries until the succeeding stage of pro-œstrum.

With the advent of "pro-œstrum" or "coming on heat" functional activity of the sexual apparatus is initiated. The ripe follicles project on the surface of the ovary and coincidently with their full development the endometrium exhibits evidence of increased growth and vascularity. The glands secrete, and the congestion of the stroma is so great that rupture of the thin-walled capillaries occurs with extravasation of blood into the surrounding tissue. This extravasation and flushing of the endometrium with blood is so extreme that not only does it occasionally lead to disruption of the glands and the appearance of red cells in their lumina, but also in some animals, as the bitch, to a partial breach of surface of the endometrium and the appearance of external hæmorrhage per vaginam. We must note, however, that although pro-œstrum is always associated with increased vascularity of the endometrium and glandular activity, it is only in a few mammalian types that hyperæmia is so extreme as to give rise to external hæmorrhage from the uterus. The more common phenomena is profuse secretion of the glands only, with a slight superficial desquamation of the cornified cells of the vagina. The appearance of these cornified cells in the secretion contained in the vagina has been made use of by Papanicolau, Wright and Dodds, and others as evidence of pro-œstrum in their investigations of the sexual cycle in rodents.

Pro-œstrum is followed directly by œstrum, which in the majority of mammals is the period when coition occurs. It is also in many animals, but by no means all, the point in the sex cycle when ovulation occurs from the ripe follicle. Œstrum lasts from a few hours, as in the sheep, to about a week in the case of the bitch. It is interesting to note in types where no denudation of the endometrium occurs during pro-œstrum that œstrum is comparatively a short period, as compared with other animals as the bitch, where regeneration of tissue is necessary. During œstrum activity of the uterine glands continues and the uterine cavity contains much secretion. Leucocytes take the place of the "cornified cells" in the vagina, and their presence is an indication of the onset of this stage.

Now, if fertilisation does not occur, a state of pseudo-pregnancy supervenes, which is of particular interest to us as gynæcologists. This state, in essential anatomical details so far as the ovary, uterus, and mammary glands are concerned, resembles a condition of true pregnancy. The variation is merely one of degree.

In the ovary the corpus luteum resulting from the ruptured Graafian follicle persists throughout pseudo-pregnancy and towards the end of the period assumes the yellow colour due to the lutein lipoid. The uterus exhibits *increased* vascularity, and the endometrium, both stroma and glands, undergoes considerable hypertrophy. This hypertrophy in both macroscopic and microscopic detail is to be regarded as an early decidua. The retention of secretion of the uterine glands may, in fact, be the equivalent of what in pregnant ungulates is known as "uterine milk," a possible source of nutrition to the developing ovum. In this connexion I would ask you to remember the high calcium content of the secretion of the corporeal uterine glands. If it is not required by pregnancy it is discarded, and this accounts for the high calcium.

content in the menstrual lochia of the human female.

At the end of pseudo-pregnancy, the actual duration of which is a very variable quantity in different animals, a stage of involution sets in characterised by degeneration of the endometrium or decidua, and in some instances by definite necrosis associated with hæmorrhage. In the bitch, whilst bleeding occurs at this stage also into the tissues of the endometrium, there is no external hæmorrhage. In other mammals —e.g., the cow—a definite post-œstral hæmorrhage occurs, forming the so-called "menstrual clot." This is thought by Hammond to coincide with the termination of a short pseudo-pregnancy, and he is probably right. When the pseudo-pregnancy is short it will be readily understood that hæmorrhage is more likely to be a feature of the tissue necrosis that follows its termination, owing to the embryonic state of the pseudo-decidua.

We therefore arrive at the very important observation that in the mammalia hæmorrhage from the genital tract can and does occur in different species at the following points in the sexual cycle.

(1) During pro-œstrum, as a result of the local hyperæmia of the endometrium incidental to this physiological state —cf. the bitch.

(2) At the end of pseudo-pregnancy, resulting from degeneration of the false decidua and necrosis of this structure —cf. the cow.

In other types—e.g., the sheep, sow, mare, and various rodents—no external hæmorrhage into the uterine cavity occurs at all, either during the stage of pro-œstral congestion or during involution at the end of pseudo-pregnancy. Now the mammalia naturally fall into two well-defined groups:—

(*a*) Species in which the sexual season is associated with but one complete œstral cycle—the so-called "mon-œstrus type" of Heape.

(*b*) Animals in which there is a recurrence of short œstral cycles at regular intervals throughout the sexual season—the "poly-œstrus type."

Amongst poly-œstral types much variation exists, both in duration and kind, with regard to the various units of the œstral cycle. Generally speaking, however, it may be said that the sex cycle of the poly-œstral animal differs from that of the mon-œstral in the following particulars:—

1. Anœstrum may be absent, as in the primates.

2. Pro-œstrum is short and, in practically all species, is characterised only by congestion of the endometrium with increased activity of the uterine glands, but *no external hæmorrhage.*

(3) Œstrum is very short and may be only a matter of a few hours.

(4) Pseudo-pregnancy is also abbreviated, and its termination may be associated with hæmorrhage from the uterine cavity.

N.B.—The brief pseudo-pregnancy between the recurring short cycles of poly-œstral animals was wrongly regarded by Heape as being a short rest period and called by him the "di-œstrum." Using the same terminology Heape calls the short sex cycle of the poly-œstral mammal the "di-œstrus cycle."

Although the poly-œstral state occurs naturally in certain wild species, particularly rodents, it is a fact that in domestic types it appears to be the direct outcome of selective breeding, altered feeding, and changed environment. Marshall has drawn attention to the fact that whilst the wild sheep is mon-œstral, the Scottish "blackface" in the Highlands has two di-œstral cycles in the sexual season. The same breed under the improved conditions of the lowlands increases the cycles to five or six. On the other hand, various English breeds—e.g., the "Dorset horn"—exhibit still further activity and frequently have two sets of lambs in the year. With the merinos of New South Wales the di-œstral cycles succeed one another throughout the year and there is a complete absence of anœstrum. The purpose of such extreme cyclical sex activity is, of course, to increase the possibility of pregnancy, and so promote the fecundity of the species. The artificial development of the poly-œstral from the mon-œstral type as a result of feeding and environment is an interesting and important aspect of comparative physiology to the gynæcologist. Recently Beaumont and Dodds have shown the importance which certain foods rich in vitamin E—e.g., wheat, peas, lettuce, &c.—have upon the reproductive function. It is, I think, rather an interesting coincidence that in the arid tracts of the Sahara the only sustenance available for the herds of goats is a food particularly rich in this vitamin—viz., the Alfa grass.

OVULATION AND THE SEX CYCLE.

Let us next consider the position that ovulation occupies in the sexual cycle. In the majority of poly-œstral animals, rupture of the Graafian follicle occurs either during or shortly after œstrus. In a few types —e.g., the rabbit and cat—pro-œstrum and œstrum are apparently fused, and ovulation *only* occurs a few hours after coitus. In the absence of coitus there is no dehiscence and no formation of a corpus luteum. Under these conditions pseudo-pregnancy is absent and a prolonged œstrus passes insensibly into a state of anœstrum. The unruptured follicles in the ovary become atretic and degenerate, with hæmorrhage into their cavities, a fact of considerable interest in a possible similar production of fibrocystic ovaries in the human female.

When coitus occurs with a vasectomised male in the case of the rabbit or cat, a corpus luteum forms as usual, followed by the characteristic decidual development associated with pseudo-pregnancy.

In the primates a degree of complexity is found with regard to the sexual cycle and ovulation which appears to have caused some difficulty in the proper interpretation and appreciation of the physiological facts accompanying the clinical phenomena. In both man and monkeys the sexual life of the female from puberty to the menopause consists of a constantly recurring series of short œstral cycles. There is no anœstrum, and the sexual cycles are consecutive and continuous. There appears to be no doubt, however, that each cycle, as in other poly-œstral types, consists of a pro-œstrum, œstrum, and a pseudo-pregnancy.

Although monkeys exhibit an unbroken succession of such cycles, it is very interesting to find that in certain types breeding is restricted to certain periods of the year. It is evident, therefore, that *fertile* ovulation must be carefully considered as being a phenomenon apart from pro-œstrum. Corner has made the observation that in some monkeys when ovulation has not taken place and there is consequently no corpus luteum and pseudo-pregnancy, menstrual hyperæmia still occurs.

Ovulation in the monkey, according to Corner's observations, takes place between the fourteenth and sixteenth days of the menstrual or sexual cycle. This corresponds to the recent work on the human species by W. Shaw and others who, by a study of the life-history of the corpus luteum, have proved that ovulation in *homo* occurs between the thirteenth and seventeenth days of the menstrual cycle. Ovulation in both man and monkeys is generally independent of coition. I say "generally" because in some fibrocystic ovaries examined from single women I have on occasion failed to find any evidence of recent or remote lutein tissue. May it be suggested that this is an atavistic state of sexual function?

In both man and monkeys under domesticated and, therefore, artificial conditions, coitus occurs at any time during the menstrual cycle. There is some evidence that a short œstral period does occur in the human female immediately after the menstrual function, but generally speaking it appears to be independent of the sexual cycle. In fact, as we know, the sexual stimulus persists after complete ablation of the essential sexual organs, at any rate during the period of active sexual life. As Marshall has pointed out, luxurious conditions favour the prolongation of

œstrum, and "in some of the lower animals when stimulated by abundant food-supply (e.g., domesticated rabbits) coition often occurs during early pregnancy, when it can serve no purpose in perpetuating the race."

In the human species the difficulties which arise in arriving at a proper conception of the menstrual function are minimised, I think, if we remember that pro-œstrum and œstrum provide one set of phenomena. Ovulation and pseudo-pregnancy provide another. In the human female the picture is complicated by the very simple fact that both sets of phenomena overlap.

Ovulation occurs between the thirteenth and seventeenth days of the menstrual cycle. This observation of Schroeder's and W. Shaw's I have repeatedly confirmed from the investigation of ovaries in relation with the menstrual cycle in a series of laparotomies performed for various indications.

From the date of ovulation a state of pseudo-pregnancy exists until its termination about the twenty-eighth day of the period, when necrosis of the menstrual decidua takes place and external hæmorrhage commences. Pari passu with the period of completion of the pseudo-pregnancy a state of pro-œstrum develops which reaches its acme also about the twenty-eighth day of the cycle, but persists during the abortion of the pseudo-pregnancy. This is followed at the conclusion of the menstrual hæmorrhage by a short œstral period, Nature's provision to promote fertilisation of the ovum about to be liberated from one of the succeeding follicles undergoing maturation.

The menstrual discharge in the human female, therefore, normally contains blood derived from the endometrium as a result of two distinct factors:—

(*a*) Hæmorrhage resulting from necrosis of the endometrium caused by abortion of the pseudo-pregnant decidua.
(*b*) Blood produced by rupture of the capillaries caused by pro-œstral hyperæmia.

Appreciation of this fact—viz., that menstruation in the primates is a composite process involving two separate and distinct functions, each subserving a special physiological purpose, but overlapping the other in order to secure the maximum effect in the shortest time, throws considerable light upon what otherwise is a complex and difficult problem.

I will give you an analogy. The menstrual function may be compared with the stage of a theatre between two acts. One set of scene-shifters are busy removing the paraphernalia of the last scene whilst *another* are engaged in the same place and at the same time in reconstruction for the next act. Both are working together at top pressure and occasionally, I am afraid, one gets in the way of the other!

Now it is possible to study both sets of phenomena independently, and in considering the recent work that has been and is being done on the menstrual function, it is important to keep this distinction well to the front. My own observations, like those of Frankel, Halban, Schroeder, W. Shaw, and others, are more concerned with the investigation of what may be termed the "pseudo-pregnant" aspect of menstruation. On the other hand, the work of Adler, Allen and Doisy, Marshall and Dixon, and Dodds and Wright has been mainly in relation with the isolation and function of the hormone which produces "pro-œstrum" and "œstrum."

It is unnecessary to detail at any length the anatomical features of the human endometrium at different stages of the sexual cycle. The appearance of the so-called "constructive," "destructive," and resting stages are sufficiently well known. Too much stress, however, has, I think, been laid upon the sharp demarcation of these phases. It is far more important to remember that the endometrium in health from puberty to the completed menopause is never actually at rest. It is always either functioning or preparing to function. As Schroeder has pointed out, there is evidence of commencing secretory activity of the uterine glands from about the thirteenth to the seventeenth day of the menstrual cycle. This activity increases, but as I have shown elsewhere, there is also an increasing *retention* of secretion as the cycle advances, owing to constriction of the ducts by the developing decidual cells of the stratum compactum. It is not until some necrosis of the stratum compactum occurs on the first day of the menstrual function that there is a sudden out-pouring of the pent-up secretion.

As a matter of fact, a few dilated glands with "fern-like" processes are constantly to be seen in sections of the endometrium from the seventeenth day of the cycle onwards. They, of course, become more numerous as the length of the cycle increases owing to the construction of more ducts. In the fully developed menstrual decidua these dilated glands form a very distinct feature in transverse sections through the uterine cavity, and constitute the "stratum spongiosum." With the complete development of the "stratum compactum" it will be understood that liberation of the corporeal secretion is not possible until necrosis of the superficial layers of the endometrium has removed the constriction of the ducts.

This is an important fact in view of the criticism that the formation of a menstrual clot is a normal part of the physiological mechanism of the menstrual function in the human female. It has been contended that the formation of a thrombus is impossible in the presence of a thrombolysin. The answer to this criticism is that the thrombolysin contained in the secretion of the uterine glands is not liberated until the thrombus is already formed.

That a menstrual clot in the uterine cavity *is* formed during the process of molecular necrosis of the menstrual decidua is certain; the original observation has been repeated on several occasions, and it has been confirmed by W. Shaw and others. It is also equally certain that the menstrual lochia in health contains frequently no clots, although it is by no means uncommon to find in the discharge very small thrombi in process of disintegration. The discharge normally consists of the products of endometrial necrosis and autolysis with the secretion of the corporeal glands. It therefore contains no fibrin or fibrinogen, but it does contain a high percentage of calcium, possibly necessary should pregnancy occur, but otherwise discarded.

Relation of the Corpus Luteum to the Menstrual Decidua.

During the last quarter of a century a great deal of work has been done in the investigation of the structure and life-history of the corpus luteum, and especially the relation of this body to the menstrual function.

To Fränkel belongs the credit of first drawing attention to the relationship which exists between the corpus luteum and menstruation. By destroying the corpus luteum with the actual cautery he altered the menstrual rhythm, and in the case of pregnant animals he produced abortion. As a result of these experiments Fränkel came to the conclusion that the function of the corpus luteum was to maintain the nutrition of the uterus from puberty onwards, and to prepare the endometrium for the embedding of the ovum. He also thought that the lutein hormone was responsible for the local hyperæmia which accompanies menstruation. Fränkel's work was criticised chiefly on the basis that the cautery did not destroy all the lutein tissue in the ovary.

Halban, therefore, carried the investigation a step further by actually excising the corpus luteum in 40 cases. He found that uterine hæmorrhage occurred in 92·5 per cent. of the cases so treated. Strangely enough, however, this observer made no attempt to correlate the hæmorrhage with menstruation, and, in fact, came to the conclusion that the menstrual function was not due to the corpus luteum but to ovulation! Halban thought that the lutein hormone exerted an inhibitory effect both upon menstruation and ovulation.

Myer and Ruge, Miller and Schroeder, however, by studying the development of corpora lutea in relation with the anatomical appearances of the endometrium brought forward evidence in support of Fränkel's original thesis. Schroeder, in fact, pointed out that whilst a young corpus luteum is always present at the commencement of endometrial activity, a mature corpus luteum is associated with what is generally recognised as the premenstrual state of the endometrium. Furthermore, degeneration of the corpus luteum is found during the period of active endometrial necrosis.

This was the position when, in 1926, I decided to repeat Halban's experiments, and at the same time to make a careful study of the endometrium should uterine hæmorrhage occur. The result of my first observation, described in detail in the *Journal of Obstetrics and Gynecology*, vol. xxxiii., No. 3, was to convince me that the effect of excision of the corpus luteum was to produce necrosis of the uterine endometrium. Material was obtained which proved quite conclusively that the uterine hæmorrhage artificially produced on the eighteenth day of the menstrual cycle by excision of the corpus luteum 39 hours previously, was in essential details identical with that of the "menstrual period." I had, in fact, antedated the normal function by ten days. More interesting still, the next "period" did not occur until 44 days later, or only four days later than it would have occurred had no interference with the rhythm taken place. Since this paper was published further observations have been made, and I am now able to carry the deductions a step further.

Twelve more opportunities have occurred of excising the corpus luteum at periods varying between the seventeenth and twenty-fifth days of the menstrual cycle, and in every instance uterine hæmorrhage with endometrial necrosis has followed within 36–48 hours of the operation. In each case also the next following menstrual period occurred within a few days of the normal period, had no experimental interference taken place. In other words, the only alteration of the rhythm was to antedate the menstrual period directly in proportion to the date on which removal of the corpus luteum was effected.

Examination of the corpora lutea which were removed showed that this structure is *normally a cystic body*, and that, although there is much proliferation of the cells of the tunica granulosa with resultant thickening of the wall, a cavity is always present containing a clear fluid. The point of rupture of the parent follicle is usually evident on the surface of the corpus luteum as a small dimple or scar. The aperture is apparently closed by approximation of the growing cells of the tunica granulosa, now accepted as being identical in type with the large lutein cells of the fully developed corpus.

The corpus luteum increases in size, but maintains the same grey cystic appearance until immediately before the onset of the menstrual abortion. Lipoid degeneration then occurs, characterised by the appearance of the yellow pigment in the cells and hæmorrhage in the cavity. Hæmorrhage is the result of degeneration and fatty necrosis, and not a sequel of dehiscence of the follicle. For this observation we are indebted to Wilfred Shaw, and with his views on this point I entirely agree.

The cause of lutein degeneration in association with menstruation is still a problem. My own view is that it is closely related with death of the unfertilised ovum. I have recently suggested that it is the result of a "negative" phase initiated by the vaccine action of the unfertilised dead ovum and the cells of the corona radiata, cells morphologically identical with the large cells of the corpus luteum.

RELATION OF THE GRAAFIAN FOLLICLE TO THE MENSTRUAL FUNCTION.

It is evident from the results of excision of the functionally active corpus luteum that this body exerts an important influence upon the development of the endometrium. In fact, it appears that the growth of the menstrual decidua is entirely dependent upon its proper function, and that withdrawal of its active principle is followed within 48 hours by necrosis of the endometrium. It appeared a matter of interest, therefore, to study the effect of similar investigations in relation with the Graafian follicle before its rupture on the thirteenth day of the cycle.

On three occasions the opportunity was taken to destroy developing follicles before maturity by "needling" both ovaries. It was found on each occasion that uterine hæmorrhage commenced within 48 to 72 hours of the operation. All the investigations were made before the thirteenth day of the menstrual cycle and in the absence of any functioning corpus luteum. These observations were interesting, but were regarded as inconclusive, since it was thought possible that the uterine hæmorrhage might be the result of pro-œstral congestion resulting from the peritoneal absorption of a follicular hormone.

A further series of four observations were made of excising large Graafian follicles either by double or single partial oöphorectomy. In three out of the four cases uterine hæmorrhage began within 72 hours of the operation. In these three cases the excision took place between the tenth and thirteenth days of the cycle. In the patient where no hæmorrhage occurred the operation was performed on the seventh day of the cycle or three days after the termination of a four-day period. It was concluded, therefore, from this second series of observations that the uterine hæmorrhage occurring in the first group *was* due to the destruction of the follicle and not to the absorption of follicular hormone.

In the case of the three patients whose ovaries had been "needled" the opportunity was taken of collecting some of the liquor folliculi, and amounts varying between ½ c.cm. to 1 c.cm. were injected intravenously into other patients without producing any obvious clinical effect. The uterine hæmorrhage produced by excision of Graafian follicles differed somewhat in type from that produced by removal of the corpus luteum. It was comparatively slight, somewhat irregular, and continued seven to ten days—in fact, longer than the usual menstrual bleeding and comparable with the pathological type which I have called "menostaxis" as distinct from "menorrhagia."

These observations point to the fact that not only the corpus luteum but also the Graafian follicle is responsible for the growth of the endometrium, which certainly appears logical owing to the development of the former from the cells of the latter.

The follicular hormone, therefore, appears to be a complex body possessing more than one active principle. That it contains a body capable of producing œstrus in the lower animals has been proved conclusively by the work of Adler, Fellner, Herrmann and Fränkel, Allen and Doisy, Stockhard and Papanicolau. Recently Dickens, Dodds, and Wright have isolated a physiological principle in the form of an oil which stimulates œstrus in rats and which has a marked depressor action.

It is only reasonable to suppose that a similar œstrus-producing principle is present in the ovaries of women, although actual physiological proof is as yet required. There is certainly no evidence available to prove that the intravenous injection of liquor folliculi has any influence in the production of the menstrual hæmorrhage in the human female. In fact, my observations all tend to show that the uterine bleeding is produced as the result of endometrial necrosis by the withdrawal from the circulation of some principle elaborated by the follicle and the corpus luteum which is essential for its development.

The œstrus-producing hormone of Dickens, Dodds, and Wright obtained from pigs' ovaries was not, however, confined to the liquor folliculi. It was present in extracts from the whole ovaries, and these workers state definitely that their findings do not support the contention of Allen and Doisy that the active principle is mainly a feature of the liquor folliculi. Allen and Doisy themselves did not find it in extracts

of the corpus luteum. On the other hand, Samson Wright has informed me that he and his co-workers have isolated the hormone not only from the ovaries but also from the placenta and various other tissues submitted to them from the gynæcological operating theatre.

In 1914 I called attention to the presence of an œstrus-producing hormone in the uterine secretion of rodents, and it seems probable that the existence of this active principle is only dependent upon the ovaries in a secondary sense. It may, indeed, be produced in tissues other than the ovaries—e.g., the thyroid—as is evidenced in the human species by the persistence of the sexual instinct after complete ablation of the uterus and ovaries, or the occasional occurrence of endometrial congestion and hæmorrhage at a considerable period after double oöphorectomy.

The result of clinical investigation on human ovaries has brought to light, therefore, the following facts:—

(1) That removal of the physiologically active corpus luteum at any stage of its development during the menstrual cycle is followed directly by molecular necrosis of the endometrium.

(2) That destruction of mature Graafian follicles before rupture is also followed by endometrial necrosis.

(3) That excision of mature Graafian follicles likewise results in necrosis of the endometrium.

(4) That injection of liquor folliculi does not produce uterine hæmorrhage.

It is evident, therefore, that both the Graafian follicle and the corpus luteum contain an active principle which is essential for the proper development and function of the endometrium. If it is withdrawn from the circulation necrosis of the superficial layers of the endometrium ensues. On the other hand, its constant stimulus promotes development of the endometrium until the mature decidua is formed.

This active principle is probably produced from the cells of the tunica granulosa, and, inasmuch as it is a feature of the secretion of both the follicle and corpus luteum, neither the name "folliculin" nor "lutein" appears entirely suitable. As an alternative I suggest the term "*ovarin*" to designate the hormone which is essential for the proper growth and function of the endometrial stroma.

The recently introduced term "œstrin" should be reserved for the other œstrus-producing hormone of the follicle which experiment shows is not present in the corpus luteum. "Œstrin" is probably responsible for the pre-menstrual congestion and functional activity of the uterine glands. "Ovarin," on the other hand, controls the growth of the stroma, and the withdrawal of this hormone from the circulation initiates endometrial necrosis with hæmorrhage from the congested stroma.

The significance of this conception of the menstrual function has, I think, an important corollary in the explanation of some cases of pathological uterine hæmorrhage. If endometrial necrosis ensues upon the destruction or excision of the maturing follicle and the corpus luteum, it is reasonable to suppose that similar trauma effected by disease is followed by like results. This is, indeed, the case, and many instances of irregular uterine hæmorrhage in association with fibrocystic ovaries, prolapsed ovaries, and chronic inflammatory disease of the uterine adnexa are, I think, due to the death of maturing Graafian follicles and pathological corpora lutea. Recently I have investigated several ovaries from cases of large fibroids where metrostaxis as well as menorrhagia has been a feature, and in every instance I have found large cystic unruptured follicles, as well as corpora lutea in various stages of degeneration. The follicular or lutein cysts in many instances contained blood. It seems probable, therefore, that in these cases both the uterine hæmorrhage and the sterility have a common ovarian origin. The sterility is due to unruptured follicles and the metrostaxis to the periodical irregular cutting off of the supply of "ovarin." It is in these and similar cases infinitely better for a Graafian follicle never to develop at all. Partial maturity with subsequent death is probably always associated with endometrial necrosis and hæmorrhage, such as is commonly found during the years of the menopause, and at puberty. Excess of the "ovarin" hormone is, I think, one of the causes of precocious decidual development and, as I have shown elsewhere, it appears to be a factor in the production of severe menstrual pain.

CONCLUSION.

In conclusion, may I say just a word with regard to the therapeutic value of so-called ovarian and lutein extracts. I am afraid that I cannot claim hitherto to have had any considerable and *sustained* success with any single extract at present on the market. This is more particularly the case in the control of irregular functional uterine hæmorrhage—metrostaxis in other words. Every now and again one has an apparent success, and then in another case with precisely a similar pathological picture and using the same commercial preparation no result whatsoever is obtained. Now, I think that the cause of these discrepancies lies in the fact that in the first place whole animal ovaries are used in the preparation of the extract. In the second place I doubt very much whether many commercial extracts are made when "ovarin" is present in the organs used. For a preparation to have any physiological action in the prevention of premature endometrial necrosis and, therefore, hæmorrhage, it should be made either from *mature* Graafian follicles or from *functioning* corpora lutea—not the degenerated "yellow bodies" which are but the empty shell and from which the inmate has escaped.

Not until extracts are always made from animals' ovaries during either pro-œstrum or the early months of pregnancy do I expect, on physiological grounds, to obtain uniformly satisfactory therapeutic results.

SOME DIFFICULTIES IN THE DIAGNOSIS OF ACUTE LEUKÆMIA.

BY J. B. DAVEY, M.B. LOND., D.T.M. LIVERP.,
HONORARY PATHOLOGIST TO THE CHELTENHAM GENERAL AND EYE HOSPITAL;
AND
L. E. H. WHITBY, *M.C.*, M.B. CAMB., D.P.H.,
ASSISTANT PATHOLOGIST, THE MIDDLESEX HOSPITAL.

IN reviewing the clinical and pathological aspects of the six cases of acute leukæmia that have come to our notice in the past 18 months, the increase in the incidence of all types of leukæmia has been rendered more noticeable. It seems unlikely that the advent, within so short a time, of three cases of the rare acute lymphatic type of the disease should be coincidence. During the same period, of the more chronic forms, no less than 13 cases of lymphatic leukæmia and 11 cases of myelocytic leukæmia have been examined and diagnosed at the Middlesex Hospital, whilst Prof. Sholto Douglas[1] has drawn attention to the large numbers of cases occurring at Sheffield during recent years and suggested the possibility of the disease being sometimes epidemic.

In describing and labelling these cases we are at the outset confronted with the lack of agreement of various authorities with regard to the incidence of the various forms and the means of differentiating them. Some of the opinions may be quoted here. Thursfield[2] does not distinguish the various types of acute leukæmia, and says "the lymphocyte of acute leukæmia is not the lymphocyte of the normal blood and is probably (Cabot) a marrow rather than a lymph gland cell." Gulland and Goodall[3] state that myeloblastic (acute) leukæmia is the more frequent and that acute lymphatic leukæmia is very rare and only distinguished from the myeloblastic variety by

the Jenner-Giemsa method of staining—a process which the authors describe as "a rather tricky exercise in staining gymnastics." With this opinion we concur.

In another publication Gulland [4] writes that "the acute myeloblastic and lymphatic forms (of leukæmia) are probably the most common," but at a later date he [5] is reported as stating, "I am becoming somewhat sceptical of the existence of a really acute lymphatic form." He explains this attitude by the fact that many of the myeloblastic cases are definitely mixed at the outset and only become purely myeloblastic in the terminal stage. MacCallum's [6] experience is that acute lymphoid leukæmia is more common than the chronic form but that the cells are larger and that some cases formerly classified as acute lymphatic are now known to be myeloid. Todd,[7] under acute myelogenous leukæmia, says, "the predominating leucocyte is the most immature member of the bone-marrow series—i.e., the myeloblast." He mentions that in some cases the cells are so very immature that the oxidase test fails, and it may be impossible to distinguish the disease from acute lymphatic leukæmia.

A consideration of the origin of the various forms of leucocyte might be expected to throw some light on the immature cells found in the leukæmias, but here again there are different schools of thought—some adhering to a monophylitic and others to a polyphylitic theory. The subject is therefore one of some difficulty, and we can only hope with Gulland that some more satisfactory method of differentiating large immature leucocytes than the Jenner-Giemsa stain and the oxidase reaction will be devised. We consider Lambright's [8] method of oxidase staining a great improvement on Goodpasteur's, and we are indebted to Dr. J. Allman Powell for drawing our attention to the method.

With these cases of leukæmia we have included one of glandular fever for, as the account will show, it presented in the early stages very real difficulties of diagnosis, and it is possible that sporadic cases such as the one described are more common than is supposed.

CASE 1. *Acute Lymphatic Leukæmia.*—A man, aged 53, was admitted to the Middlesex Hospital on June 4th, 1926, under Dr. R. A. Young. He died five days after admission, the duration of life from the initial symptoms of headache and sweating being six weeks. He was constipated throughout his whole illness and whilst in hospital enemata produced only small blood-stained results.

On admission the skin was of pale lemon colour, the mucous membranes were pale; there were purpuric spots on the abdomen, and a large subcutaneous hæmorrhage under the right eye. There was profuse hæmaturia (which had been present for two days prior to admission) and bleeding from the gums. The spleen was just palpable and there was tenderness below the liver. There was no glandular enlargement. Temperature 99° F., pulse 90, respirations 26.

During the five days the patient was under observation he became progressively weaker, vomited frequently, and had a subnormal swinging temperature. Blood cultures were sterile and the only blood count performed gave the following result: hæmoglobin, 28 per cent.; red cells, 1,104,000; colour-index, 1·3; leucocytes, 10,200; polymorphonuclears, 26 per cent.; lymphocytes, 68 per cent.; large mononuclears, 6 per cent. Two normoblasts per 100 leucocytes, poikilocytosis, and a fair number of polychromatic cells. About 75 per cent. of the lymphocytes were of large-cell type and large numbers of cells consisted only of "smeared nuclei." Goodpasteur's oxidase stain gave a negative result for oxidase granules.

This is a typical case of acute leukæmia and it is noteworthy that the patient was a medical man who had worked with X rays for many years. Gulland [4] records a case of a woman who had extensive X ray treatment for malignant metastases and who had a large spleen with a blood picture of acute myelocythæmia; the blood count and spleen returned to normal after cessation of the X ray treatment. It is possible, therefore, that our case resulted from the prolonged X ray exposure inducing a leucoblastic crisis.

Many hæmatologists deny the existence of an acute lymphatic leukæmia of large-celled type owing to the acknowledged difficulty in distinguishing the cells from myeloblasts. Oxidase staining is admittedly often unsatisfactory, but when carefully controlled with normal and with known pathological blood it is certainly of value. In diagnosing this case as acute lymphatic leukæmia rather than myeloblastic, we base our opinion on the negative oxidase reaction, the presence of "smeared nuclei," and the scantiness of abnormal red cells, particularly megaloblasts and macrocytes—a factor usually well marked in myeloblastic and myelocytic leukæmia. There is no doubt that this case was not a terminal phase of the more chronic type as the patient, on account of his occupation, had had his blood examined at regular intervals.

CASE 2.

Date in 1926.	Hæmoglobin per cent.	Red cells.	Colour index.	Leucocytes.	Polymorphonuclear per cent.	Lymphocytes per cent.	Nucleated reds.	Remarks.
April 7th ..	30	1,176,000	1·4	196,800	2	98	0	Poikilocytosis present. Predominant cell large lymphocyte (70 per cent.).
„ 21st ..	30	1,950,000	1·5	222,000	1	99	0	Poikilocytosis. Large lymphocytes (70 %).
„ 29th ..	20	620,000	1·7	167,000	1	99	2 megaloblasts.	Poikilocytosis and macrocytes. Radium applied five days previous to count. Large lymphocytes (50 per cent.).
May 6th ..	22	770,000	1·5	135,000	3	97	2 megaloblasts.	Poikilocytosis and macrocytes. Predominant cell small lymphocytes (60 %).
„ 14th ..	16	1,700,000	0·5	96,600	1	99	2 megaloblasts, 1 normoblast.	Poikilocytes, macrocytes. Death five days later. Predominant cell large lymphocytes (70 per cent.).

CASE 2. *Probably the Terminal Crisis of a Chronic Lymphatic Leukæmia.*—A man, aged 32, was admitted to the Middlesex Hospital on April 7th, 1926, under Dr. C. E. Lakin. He died six weeks afterwards, the duration of symptoms prior to admission being three weeks. He had first noticed bleeding from the gums, bilateral parotid swellings, sweating, loss of hearing, and increasing weakness.

On admission the gums were swollen, red, and bleeding, perspiration was profuse, and the patient was very deaf. Temperature 100° F., pulse 140, respirations 24. The spleen was greatly enlarged and the liver was palpable one finger-breadth below the costal margin. Cervical, axillary, and inguinal glands were enlarged and the tonsils and adenoids (probably accounting for the deafness) were very much hypertrophied. Retinal hæmorrhages were present. All the glandular swellings, including the spleen, were remarkably soft.

The clinical course of the case was marked by an evening temperature varying from 100° to 101·5°, periodic attacks of dyspnœa, enlargement of the veins over the chest, and obstinate bleeding from the gums.

Treatment included mouth washes, liquor arsenicalis, and the application of radium over the splenic area, but the latter resulted in so great a destruction of red cells that it was discontinued.

Blood cultures were sterile. The sedimentation of red corpuscles was 7·5 c.cm. There was a very marked thrombopenia and a great tendency for the blood to agglutinate as soon as a drop was placed on a slide. The patient belonged to Group II. of the blood groups. In

view of the marked auto-agglutinating power of his serum, it was tested against normal red cells of Group II., but without any effect. The record of blood examinations was as under:—

As in Case 1, the predominant cell was (with the one exception commented on below) always a large lymphocyte, and of these quite 50 per cent. were present as "smeared nuclei." Both Goodpasteur's and Lambright's oxidase staining reactions were negative.

The most interesting feature of the case was the result of the application of radium to the splenic area. The rather drastic effect on the red cells was not unexpected, but the marked alteration in the leucocytic picture—from large to small lymphocyte predominance—was not foreseen. The blood picture reverted to its former type a week later—that is, within 20 days of the application of radium.

In assuming the case to be the terminal phase of an old-standing case rather than a primary acute leukæmia, we are influenced by the clinical and hæmatological findings rather than by the history. Chronic lymphatic leukæmia often exists for years without symptoms, and it is probable that most cases which have high leucocyte counts and large spleens are of long standing. The changes in the red cells were characteristic of lymphatic rather than myeloblastic—viz., reduction in numbers and in hæmoglobin rather than by the appearance of grossly abnormal cells.

CASE 3. *Acute Myeloblastic Leukæmia.*—A man, aged 34, was admitted to the Middlesex Hospital on Feb. 4th, 1925, under Dr. C. E. Lakin. He died two weeks after admission, the time from the onset of symptoms to death being five weeks. He first attended the dental hospital on account of swelling and bleeding of the gums and soon after noticed a swelling in the neck which was followed by purpuric spots on the abdomen.

On admission the gums were necrotic and bleeding; there were large, soft glands in the neck and a few small discrete, hard, painless glands in the axillæ and groins; there were purpuric spots on the abdomen and legs. The spleen was palpable two fingers-breadth below the costal margin. Temperature 101° F., pulse 104, respirations 22. The clinical course was marked by an evening rise of temperature reaching 101°, and progressive necrosis of the gums. There was suppression of urine during the last 48 hours of life. Treatment consisted of mouth washes, arsenic, and later, ferri et ammon. cit.

Blood cultures were sterile. Cultures of the pharynx grew *B. proteus vulgaris* and streptococci. A blood count ten days before death showed: hæmoglobin, 58 per cent.; colour-index, 0·9; red cells, 3,200,000; leucocytes, 112,800; polymorphonuclears, 11 per cent.; promyelocytes, 11 per cent.; non-granular cells showing nucleoli, 34 per cent.; non-granular cells without nucleoli, 42 per cent.; large mononuclears, 2 per cent. By Goodpasteur's stain the percentage of oxidase containing leucocytes was 43; macrocytes numerous; 4 megaloblasts per 100 leucocytes.

Post-mortem Examination.—General glandular enlargement, particularly in the cervical region where the glands were soft and hæmorrhagic. Liver, 72 oz.; spleen, 16 oz.; kidneys, each 12 oz.—enlarged and pale with changes in the cortex and hæmorrhages in the pelves, causing obstruction on both sides; stomach contained altered blood and showed petechial hæmorrhages. The intestines showed hypertrophied lymphoid tissue with a few scattered petechiæ on the mucous membrane; there was great hyperplasia of the lymphoid tissue at the back of the tongue. The heart showed myocardial degeneration with a few scattered petechiæ on the pericardium. Sections of the liver, kidney, intestine, spleen, and glands showed extensive infiltration with myelocytes and promyelocytes. No lymphatic infiltration was evident.

Comment on this case is practically confined to the blood count, as the post-mortem sections gave a clear indication of its myeloblastic nature.

In analysing the differential count, the difficulty arose as to whether the "non-granular cells without nucleoli" were myeloblasts or large lymphocytes. Goodpasteur's stain was in this case no definite help, though the high percentage of oxidase containing leucocytes confirmed the fact that most of the non-granular cells were myeloblasts. It is not improbable, in view of the extensive lymphatic hyperplasia found post mortem, that at one phase of the disease it was of mixed type and that some, if not all, of the non-granular cells without nucleoli were lymphocytes. The marked changes in the red cells, despite a relatively small reduction in numbers, was a point in favour of myeloblastic rather than lymphatic leukæmia. The relatively small splenic enlargement influenced the diagnosis of primary acute myeloblastic leukæmia rather than the terminal phase of a chronic disease. The case shows features which contrast with those of Case 6.

CASE 4. *Acute Lymphatic Leukæmia.*—A single woman of 38 came under Mr. J. C. R. Braine-Hartnell in January, 1926, with an enlarged gland in the neck which had been present for one month. A week later other glandular enlargements developed in the neck, petechiæ appeared, and there was bleeding from the gums. There was no splenic enlargement. A blood examination gave the following result: hæmoglobin, 75 per cent.; red cells, 4,600,000; colour-index, 0·8; leucocytes, 21,940; polymorphonuclears, 32·6; lymphocytes, 58·0; large mononuclears, 2·8; neutrophil myelocytes, 3·4; transitional forms, 3·4; 5 normoblasts per 100 leucocytes. Her condition rapidly deteriorated and a blood examination 11 days later showed: hæmoglobin, 70 per cent.; red cells, 4,395,000; colour-index, 0·8; leucocytes, 26,300; polymorphs, 13·7; lymphocytes, 79·0; large mononuclears, 2·0; eosinophils, 0·3; mast cells, 0·7; transitional forms, 4·3; 12·5 normoblasts per 100 leucocytes. The differential count was complicated by the presence of many "smeared nuclei" and the predominant lymphocyte was of large type. The patient died after a profuse uterine hæmorrhage three days later. The total time from when the glandular enlargement was first noticed to death was therefore seven weeks.

We base our opinion that this was an acute lymphatic leukæmia on the low leucocyte count, the differential count, the absence of splenic enlargements, and the absence of gross changes in the red cells.

CASE 5. *Acute Lymphatic Leukæmia in a Child.*—A girl, aged 2 years 9 months, was admitted to the Cheltenham General Hospital under the care of Dr. F. J. Lidderdale on Nov. 13th, 1925. She died on Jan. 1st, 1926. The history related that five weeks before admission she had a fall from a sofa, having been perfectly well up to that time; a week later she complained of pain in the back and abdomen; she then "caught a cold" and her mother discovered swellings in the neck and armpits. She had difficulty in breathing and was brought to the hospital on Nov. 6th when she had definite stridor and cyanosis and looked very ill. On admission to hospital seven days later her general condition was better. Tubular breathing and some crepitations were present at the base of the left lung and there was some dyspnœa. The abdomen was prominent and the spleen much enlarged and hard, but not tender. The axillary, cervical, and inguinal glands were enlarged, firm, and discrete. She had frequency of micturition and the urine which was passed about every 10 minutes was loaded with urates. The temperature was subnormal for the greater part of her illness, but on Dec. 29th it rose to 101·8° and thereafter varied from 99° to 101°. On admission a blood examination showed hæmoglobin, 56 per cent.; red cells, 5,300,000; colour-index, 0·5; leucocytes, 109,000; polymorphonuclears, 6·8; lymphocytes, 87·6; large mononuclears, 2·4; mast cells, 0·4; myeloblasts, 2·0; neutrophil myelocytes, 0·4; transitionals, 0·4; 3 normoblasts and 0·8 megaloblasts per 100 leucocytes. Of the lymphocytes, 63·8 were small and 23·8 large. Films made six days later and stained by Goodpasteur's oxidase method showed 96·3 without oxidase and 3·7 with.

Post mortem, 12 hours after death.—Ulcerated hæmorrhagic zones at the nail bed of each thumb and some of the fingers. A small intracutaneous hæmorrhage in the right frontal region. Lymphatic glands in the anterior and posterior cervical triangles, the axillæ and groins were much enlarged. Blood was liquid in all parts of the body. Spleen, weight 12 oz., extended below the umbilicus, was firm and crushed strawberry colour on section; Malpighian bodies not distinguishable. Liver 2 lb. 10 oz., was pale on section. Right kidney 2½ oz., left kidney 1½ oz., with red fat in the renal pelvis. Alimentary tract showed no enlarged Peyer's patches. Left pleura contained 1 pint and the right 6 oz. of a blood-stained fluid. Left lung, lower lobe, collapsed. The ridges of fat between ribs and pleura were enlarged and red in colour and formed small sessile masses projecting into the pleural cavity. Heart muscle firm and pale. Valves normal. Several small hæmorrhages in the visceral pericardium. Under the sternum a greyish-white mass, showing small hæmorrhages on section, extended from the manubrium down over the heart, but neither lymphatic glands nor thymus could be detected on naked-eye examination. Sections of this substernal mass showed a loose connective

tissue in which endothelial cells were prominent, together with many small thin-walled vessels; the interstices were packed with lymphocytes; no Hassall's corpuscles seen. The marrow in the sternal end of the clavicle and in the manubrium was abundant and bright red. Smears of the marrow showed large numbers of lymphocytes and when stained by Goodpasteur's oxidase method showed very few cells containing granules; nucleated red cells and myelocytes were present in small numbers.

In commenting on this case, we note that the findings agree with those of Still,[9] who says, "Leukæmia in childhood is almost always a lymphatic type . . . the excess of lymphocytes being almost always due mainly to increase of the small lymphocyte." It is noteworthy that the duration of the case was at least nine weeks and it should therefore, strictly speaking, be classified as subacute. This may probably account for the great splenic enlargement and the somewhat high total leucocyte count, though in children both these factors are apt to be more marked in acute cases than they are in adults.

CASE 7.

Date in 1926.	Hæmoglobin.	Red cells.	Colour index.	Leucocytes.	Polymorphs.	Lymphocytes.	Mononuclears.	Eosinophils.	Red cells.	Remarks.
June 20th ..	82	4,560,000	0·9	32,900	4·6	95·0	0·4	Nil.	Nil abnormal.	Predominant large lymphocyte. Occasional questionable myeloblast present.
,, 22nd ..	84	4,960,000	0·86	32,200	7·6	89·6	2·4	0·4	,,	—
,, 22nd ..	—	—	—	—	6·0	91·6	2·0	0·4	—	By Lambright's oxidase stain.
July 5th ..	77	4,920,000	0·79	29,000	12·0	83·6	3·7	Nil.	Nil abnormal.	Mast cells (0·7 per cent.).
,, 31st ..	84	5,270,000	0·8	9,400	18·3	77·0	4·0	0·7	,,	—

CASE 6. *Acute Myeloblastic Leukæmia.*—A man, aged 26, was admitted on March 4th, 1926, to the Cheltenham General Hospital under Dr. J. Allman Powell. The first symptom, epistaxis, had appeared two weeks before his death.

History.—The patient had been in good health and followed his occupation (clerk) until at 3 A.M. his nose began to bleed. At the Cheltenham Eye, Ear and Throat Hospital the bleeding was traced to two dilated venules on the nasal septum, but despite all possible measures, blood continued to ooze from the nose thus adding to the already extreme anæmia. Seven days later he developed a right-sided tonsillitis with a temperature of 103°, and was then transferred to the General Hospital. He was extremely pale, no gross abnormality was present in the thorax or abdomen, and the spleen was not enlarged. There were a few shotty glands in the inguinal region and one external to the inflamed right tonsil. A blood examination three days after admission showed hæmoglobin, 13 per cent. (approximately); red cells, 730,000; leucocytes, 9440; polymorphs, 4·7 per cent.; myeloblasts, 70·3 per cent.; myelocytes, 7·0 per cent.; promyelocytes, 0·3 per cent.; lymphocytes, 17·4 per cent.; mononuclears, 3 per cent.; 2·3 megaloblasts and 2·7 normoblasts per 100 leucocytes. Marked anisocytosis.

The myeloblasts bore the usual close resemblance to large lymphocytes, and nucleoli were not evident in many of them, but their identity was easily confirmed by Lambright's stain, which showed 83·2 per cent. of leucocytes contained oxidase granules—a figure remarkably close to the 82·3 obtained for "true bone-marrow cells" in the Leishman-stained film.

Death occurred the next day. There was no epistaxis during the last few days of life, but the patient frequently vomited blood—mostly black, occasionally small amounts of red blood.

Post-mortem of the abdominal viscera showed no enlargement of glands or spleen; there was extreme pallor of the viscera, especially the kidneys, but sections of the latter showed no infiltration with myeloblasts. The stomach contained "coffee-ground material."

We would emphasise the definite assistance given by Lambright's stain. On comparing the myeloblasts with the large lymphocytes of Cases 4 and 5, the former showed a smaller average size and a much less clear and darker staining cell cytoplasm with no azur granules. The myeloblastic nuclei were variable in shape—round, oval, reniform, and sometimes duplicated—and many of them showed degenerative changes which probably obscured the nucleoli; on the whole, they occupied more of the cell body than did the nuclei of the large lymphocytes.

This case contrasts greatly with Case 3, yet both are manifestations of primary myeloblastic leukæmia. In Case 3 the myeloblastic process involved mainly the spleen and glands—as evidenced by their enlargement—and left the erythroblastic tissue of the bone-marrow comparatively untouched, as evidenced by the small reduction in the red cells. In Case 6 the tissue most involved was the more vulnerable bone-marrow with a resulting severe anæmia and an incapacity to recover from any hæmorrhages.

The cause of death in Case 3 was probably renal obstruction, not bone-marrow exhaustion, and the initial prognosis was therefore theoretically better; it is conceivable that if the hæmorrhages could have been arrested the patient might have settled down to a more chronic type of disease.

CASE 7. *Glandular Fever.*—A married woman, aged 26, with one child, came under the care of Dr. A. F. R. Conder on May 24th, 1926, complaining of sore-throat. Both tonsils were enlarged and reddened and small discrete glands were present in the neck. While under treatment for the sore-throat she developed a pale, measly rash on the abdomen, chest, and back, and some readily palpable occipital glands. She felt perfectly well. On June 15th her temperature was 99·4° F., pulse 80. The following day there was no change, but on the 17th she felt ill; her evening temperature was 103° and she was perspiring freely; 24 hours later the glandular swellings had increased, some being as large as hazel nuts. Her temperature was 103°, pulse 116. A blood examination performed on June 19th showed: leucocytes, 22,900; polymorphonuclears, 10·8; lymphocytes, 78·8; large mononuclears, 10·0; eosinophils, 0·4; no nucleated red cells; no poikilocytosis or anisocytosis; blood-platelets numerous; all grades from small to large lymphocytes present, the latter predominating. The blood picture suggested leukæmia, but in view of the absence of any indications of red cell destruction, a definite diagnosis was not made pending further examinations. On June 20th the rash had disappeared, leaving deep staining all over the abdomen. The patient's condition was distinctly worse; she was very weak and almost unable to sit up in bed; she vomited twice and complained of abdominal pain. There was no further enlargement of the cervical glands, but the axillary and left inguinal glands were easily palpable. There was no enlargement of the liver or spleen. (See table for blood count.)

The next day there was slight improvement in the general condition and a further blood count was performed. Dr. Letheby Tidy saw the patient on June 23rd and made a diagnosis of glandular fever, in view of the steady improvement in the general condition and the absence of changes in the red cells. By June 30th the patient was much better. The evening temperature was only a little above normal, but nocturnal perspiration was still present and the spleen easily palpable. By July 5th the patient was well enough to get out of bed. The spleen could no longer be felt, but the liver projected 1½ inches below the ribs; a blood count was performed. On July 31st the patient expressed herself as quite recovered; another blood count was performed.

The clinical features of this case, which tended to simulate acute lymphatic leukæmia, were fever, malaise, and rapid enlargement of glands and spleen; the difference was the absence of hæmorrhages. The hæmatological finding common to the two diseases

was a comparatively small but gradual increase in the total lymphocytes; the differences were the absence of destructive changes in the red cells and the decline in numbers of lymphocytes with clinical improvement.

It is noteworthy that glandular fever is frequently termed "infective mononucleosis," which implies an increase in the mononuclear cells. Such a term is a misnomer in that the increase occurs in the lymphocytes and not the large mononuclear cells.

In studying the lymphocytes of this case, one observed that the nucleus was eccentrically located and sometimes reniform. The cytoplasm was strongly basophil, contained azur granules, and sometimes showed vacuoles. The average size of cells was $14\mu \times 13\mu$ and of its nucleus $12\mu \times 10{\cdot}25\mu$. Lambright's stain was of considerable value.

No connexion with any other case of glandular fever could be traced, nor did any inmate of the house in which the patient was nursed contract the disease. The condition of the patient on June 20th gave cause for great anxiety, yet the impression gained from text-book descriptions of the disease is that of a mild pyrexial condition occurring in epidemics amongst children. Our case illustrates that the disease may occur sporadically amongst adults as a severe illness with a protracted convalescence. Whilst this case was running its course there was a series of cases of illness characterised by pyrexia, reddened fauces, and marked cervical glandular enlargement at one of the schools in the town. Two of these cases were examined and their leucocyte counts were 20,800 and 12,170, but the increase was of polymorphonuclear type.

Summary and Conclusions.

Acute leukæmia is fatal from a circle of causes; the leukæmic process invades the bone-marrow to the exclusion of erythroblastic tissue, and the accompanying hæmorrhages result in an anæmia which the reduced erythroblastic tissue cannot make good. Death occurs from anæmia and exhaustion unless the hæmorrhages previously obstruct the functions of a vital organ, such as the kidney (Case 3).

Assistance in distinguishing acute lymphatic leukæmia from acute myeloblastic leukæmia, other leukæmias, and glandular fever is given by the following points:—

1. *Splenic enlargement.*—This is not marked in the acute lymphatic leukæmia of adults, but is observed in children. It is not usually marked in acute myeloblastic leukæmia. Gross splenic enlargement in an adult suggests the terminal phase of a chronic or subacute leukæmia, either lymphatic or myelocytic, rather than a primary acute disease. Splenic enlargement is present in some cases of glandular fever.

2. *Duration of symptoms*, particularly hæmorrhages. In the primary acute leukæmias the symptoms rarely exceed a few weeks. If the symptoms have been present for a short time only and there is gross splenic enlargement, the probability is that the case is the terminal phase of a lymphatic rather than myelocytic, in that the former can exist in chronic form without symptoms for years, whereas the latter rarely does so. Hæmorrhages are absent in glandular fever.

3. *Total leucocytes.*—In the acute lymphatic leukæmia of adults the number is often within normal limits and probably rarely exceeds 30,000. In children the figure may be considerably higher. A high count in an adult suggests the terminal phase of a more chronic condition. In acute myeloblastic leukæmia the total figure may be considerably higher, but in the fulminating acute form it is usually low. In glandular fever the usual number is from 20,000 to 30,000.

4. *Type of leucocyte.*—Large type lymphocytes are characteristic of acute lymphatic leukæmia and of glandular fever. The presence of "smeared nuclei" is very characteristic of the lymphatic type. Cases with a mixed count of large lymphocytes and megaloblasts usually terminate as pure myeloblastic. Lambright's oxidase stain is more reliable than Goodpasteur's stain or the Jenner-Giemsa method for distinguishing myeloblasts from large lymphocytes.

5. *Red cells.*—Reduction in numbers and hæmoglobin is characteristic of both acute types, but is most marked in acute myeloblastic leukæmia. Numerous megaloblasts and macrocytes suggest myeloblastic; they are often present with a comparatively small reduction in numbers of cells; minor abnormalities only, such as normoblasts and poikilocytes—especially if ill-marked in spite of the severe reduction in total numbers—suggest the acute lymphatic. In both types the anæmia is rapidly progressive and the prognosis as to duration depends on the red cell count and hæmoglobin rather than the leucocyte count. Changes in the numbers of red cells and abnormal red cells are absent in glandular fever.

We are indebted to Dr. R. A. Young and Dr. C. E. Lakin, physicians to the Middlesex Hospital, and to Dr. J. C. R. Braine-Hartnell, Dr. Allman Powell, and Dr. F. J. Lidderdale, of the honorary staff of the Cheltenham General and Eye Hospital, for their permission to publish these cases.

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SULPHUR METABOLISM IN ARTHRITIS DEFORMANS.

BY A. P. CAWADIAS, O.B.E., M.D. DURH. AND PARIS, M.R.C.P. LOND.,

FORMERLY CHIEF OF MEDICAL CLINIC, PARIS UNIVERSITY, BEAUJON HOSPITAL; AND SENIOR PHYSICIAN AND LECTURER FOR CLINICAL MEDICINE, EVANGELISMOS HOSPITAL, ATHENS.

OF the three known forms of sulphur which are concerned in metabolism—mineral suphates, sulphur lipoids, and protein sulphur—it is the last which is the more important and has been exclusively studied in physiopathology.

The question which first arises is whether these sulphur-containing proteins have a separate metabolic history and a special function differing form that of the other proteins. Recent research answers in the affirmative this double question. That the metabolic history is different is shown by the fact that in certain conditions, such as inanition, convalescence, various diseases, there is not a parallel catabolism of sulphur-containing proteins, and of proteins not containing sulphur. On the other hand, whereas in the proteins of the food the ratio between sulphur and nitrogen varies between 1·7 and 14·6 : 100, the same ratio in the urine is much more fixed in the neighbourhood of 7 : 100; which shows that the organism does not catabolise all proteins indifferently, but that it catabolises the sulphur-containing proteins and the non-sulphur containing proteins, so that the two are excreted in a fairly fixed ratio.

That these sulphur-containing proteins have a definite and special function due to the sulfhydryl element has been shown by the works of de Ray Paillade, Thunberg, Heffter, and definitely demonstrated by the brilliant researches of Sir F. Gowland Hopkins. This last-named author has proved that an organic sulphur compound, glutathion,

exists in our cells and plays a very important rôle in all processes of oxidation and reduction.

It seems, therefore, interesting to study in the course of various morbid conditions troubles of sulphur metabolism, and I think that this study will give especially good results in rheumatoid arthritis in which sulphur treatment has been clinically demonstrated as very effective.

The Normal Processes of Sulphur Metabolism.

We can distinguish three phases in the normal sulphur metabolism. In the first phase, sulphur is dislocated from its protein compound under the form of imperfectly oxidised or neutral sulphur (cystine, cysteine, oxyproteic acid, &c.). About 20 per cent. of this neutral sulphur is not subjected to any further modification and is eliminated as such with the urine, and to a small extent with the fæces.

The greatest part of the neutral sulphur enters into a second metabolic phase and is thus subjected to a further modification, the oxidation. It is thus transformed into completely oxidised sulphur, that is sulphuric acid which combines with certain alkaline bases and is eliminated with the urine in the form of mineral sulphates.

A small portion of the completely oxidised sulphur is not eliminated under the form of mineral sulphates, but enters into a third metabolic phase, that of sulphoconjugation. It combines with certain toxic products derived either from putrefaction or, in general, from an abnormal metabolism of proteins, and, thanks to that combination, renders these products non-toxic. By combining with the so-called aromatic products derived from putrefaction of proteins in the intestine or from protein destruction in a focus of suppuration in the body or even from an abnormal metabolism of food and cellular proteins; it transforms these toxic aromatic products into non-toxic ethereal sulphates which are eliminated with the urine, and, by combining with the cyanates—also products of protein catabolism—it transforms them into the less toxic compounds sulfocyanates. (L. C. Maillard admits that this sulfoconjugation occurs before the phase of sulphur oxidation.)

This general metabolic progression is the same for the exogenous as well as for the endogenous sulphur-containing proteins, except for the fact that endogenous sulphur proteins stop for the greatest part in the phase of neutral sulphur. Normally, in the adult, there is a perfect sulphur equilibrium. Sulphur catabolised and eliminated on account of the normal wear and tear of our cells is replaced by exogenous sulphur. The name of Thiopexy is given to that special metabolic function of the organism through which the sulphur equilibrium is maintained. Thiopexy, sulphur oxidation, and sulphur conjugation, are the three metabolic functions of the organism regarding the sulphur. The organs which regulate this sulphur metabolism are not well known, but it is very probable—as Prof. Albert Robin and Prof. Loeper of Paris admit—that the liver plays a great rôle. Certain incomplete experimental data show also the influence of the thyroid.

Thiopexy in Arthritis Deformans.

The ideal method for the study of the function of thiopexy would consist in determining the quantity of sulphur contained in the ingesta and the quantity of sulphur excreted with the urine and the fæces, and to find out if there is an equilibrium, a positive or a negative balance.

We have adopted a more simple but more clinical method. In patients submitted to a fixed diet containing 1 g. of protein per kilo of weight of the patient, we determine the total sulphur by the Salkowski method, and the total nitrogen by the Kjehldal technique. The ratio total sulphur : total nitrogen indicates the condition of the function of thiopexy. It may be called the thiopexy index. Normally, under such conditions, an adult excretes about 2·50 of total SO_3 and the ratio total sulphur to total nitrogen is about 1 : 7 up to 1 : 10. If in that ratio the sulphur element is increased, it means that there is an increased catabolism of the sulphur-containing proteins, a loss of sulphur, or in other words a deficient thiopexy. We cannot take into consideration the cases in which the total sulphur excretion is increased, but the ratio total sulphur : total nitrogen remains normal. Under these circumstances, we have to do, perhaps, with a general increased catabolism of protein, but not with a special increased catabolism of sulphur-containing proteins.

The greatest difficulty in the interpretation of this sulphur : nitrogen coefficient arises because various authors do not agree as to its average normal value. This disagreement is due to differences in technique, not only concerning the chemical analysis but concerning also the diet to which the patient is submitted. That is why we have taken into consideration only extreme variations from the normal average. Even if we consider only these great variations, we find in rheumatoid arthritis an increase of sulphur catabolism, that is a deficient thiopexic function. Among various determinations, (made by the Salkowski method) I give the following examples:—

Kar.	Total urine SO_3 of 24 hours.	3·12 ratio S/N	1 : 3
Proc.		3·50 ,,	1 : 3
Pan.		3·72 ,,	1 : 3·5
Kots.		4·20 ,,	1 : 4·5
Pap.		3·60 ,,	1 : 2·5

Goldthwaite, Painter, and Osgood have found in one case of hypertrophic arthritis an increased thiopexy—that is, a retention of sulphur. It is probable that this indicated a defensive process. I have not met with such a retention in my numerous determinations.

Sulphur Oxidation in Arthritis Deformans.

The diagnosis of the condition of sulphur oxidation can be made by determining separately, by the method of Salkowski, the neutral sulphur and the total sulphur, and fixing the ratio neutral sulphur : total sulphur. This ratio which Albert Robin calls "coefficient of sulphur oxidation" is about 10 to 20 per cent. The relative increase of neutral sulphur does not indicate only the diminished capacity of the organism to oxidise sulphur. As Folin has shown neutral sulphur in urine represents principally the catabolism of the endogenous sulphur-containing proteins. A ratio therefore neutral sulphur—total sulphur higher than 20 : 100 does not indicate necessarily a defect in sulphur oxidation, but may also be a sign of increased endogenous sulphur catabolism.

The following are the results taken at random from determinations in patients with arthritis deformans:—

Kar.	Neutral S towards total S	17	per cent.
Ts.		21	,,
Zach.		14	,,
Proc.		18	,,
Pan.		24	,,
Kots.		16	,,
Pap.		20	,,

Bearing in mind Folin's criticism on the interpretation of this sulphur oxidation coefficient and the fact that in my determinations I have not found great variations from the highest limits of the normal standard, I think we cannot conclude to any definite trouble of sulfo-oxidation in arthritis deformans. These conclusions correct those I gave in my preliminary note two years ago when I had only a small number of determinations and had not taken into consideration the works of Folin on this subject.

Sulphoconjugation in Arthritis Deformans.

The diagnosis of sulphoconjugation is made by determining the quantity of ethereal sulphates in the 24 hours urine. My determinations were made by the Salkowski method. Here also we find divergent opinions as to the normal standard. C. Tollen finds an average of 0·18 of ethereal sulphates SO_3 in 24 hours urine. We can consider as slightly abnormal the quantities above 0·40 and as definitely abnormal the quantities above 0·60. In most cases—but not in all—of arthritis deformans the excretion of ethereal sulphates is slightly above the normal standard.

The following are certain results from my patients:—

Kar.	Ethereal sulphates in 24 hours urine	0·26
Ts.		0·24
Zach.		0·41
Proc.		0·87
Pan.		0·60
Kots.		0·58
Pap.		0·50

This slight excess of sulphoconjugation which means excess of production of aromatic products, cannot be attributed to intestinal putrefactions, because my patients did not show any clinical or coprological sign of abnormal intestinal digestion, but may be attributed either to a certain loss in chondroitin sulphuric acid, which is an important constituent of cartilage, or to an abnormal protein metabolism. Although the question is very much discussed, we have the authority of Folin for admitting that aromatic products, except indol, are not only derived from intestinal putrefactions or from putrefactions of proteins in a focus of abscess or gangrene, but that they may also be derived from an abnormal protein metabolism. In one patient the quantity of ethereal sulphates decreased distinctly after treatment with colloidal sulphur, and this coincided with a complete recovery.

General Conclusions.

In arthritis deformans sulphur oxidation is not disturbed, sulphoconjugation is in some cases slightly increased, but there is a definite inefficiency of thiopexy. In the light of these researches we can consider that the external causes of rheumatoid arthritis—microbes, toxins, or even physical conditions, such as dampness—act first on certain regulators of metabolism and principally of sulphur metabolism, regulators which are more or less predisposed. As a result of the involvement of these organs, metabolic troubles and especially sulphur metabolic troubles are elicited, and it is probable that the articular lesions are the ultimate result of these metabolic troubles.

The results of sulphur treatment demonstrated by clinical experience corroborate that conception, and I have myself seen in some patients an improvement of the thiopexic function under the influence of colloidal sulphur treatment.

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THE LATE DR. JOHN W. PINDER.—Dr. John William Pinder, who died at Horsforth, near Leeds, on June 1st at the age of 78, was well known in the district, having practised there from 1870 until his retirement some years ago. A native of Horsforth and the son of a local practitioner, he studied at the Leeds Medical School, qualifying L.S.A. Lond. in 1869 and M.R.C.S. Eng. in 1870. From 1867–69 he was assistant resident medical officer at the Leeds General Infirmary. A keen politician, he was also interested in agriculture and devoted his leisure to farming. He leaves four sons and three daughters.

RETINAL PETECHIASIS.

A CURABLE CONDITION CAUSING BLINDNESS.

ITS DESCRIPTION AND ITS BEARING ON SIMILAR LESIONS ELSEWHERE IN THE BODY.

BY H. MORELAND McCREA, O.B.E., M.D. R.U.I.

(WITH COLOURED PLATE.)

ON Jan. 14th, 1927, I read a paper before the Ophthalmological Section of the Royal Society of Medicine on Retinal Petechiasis. In that communication I drew attention to a type of hæmorrhage in the retina causing blindness, the precise nature of which had not hitherto been recognised, and in consequence its treatment had not been conducted on proper lines. The lamentable result of this incorrect diagnosis and treatment is that a number of patients are condemned to a state of blindness from which they could have been saved. I gave to this state the name retinal petechiasis and I showed that the extravasated blood had exuded from unruptured vessel walls.

The circulatory disturbances in the retina have hitherto been classified under two headings, to which I now add a third, as follows:—

1. Retinal hæmorrhage, due to rupture of the vessel walls, which occurs in elderly people whose blood-vessels show marked degenerative changes and whose blood pressures (particularly the diastolic) are almost invariably high. It is recognised that little or no treatment can benefit this condition.

2. Retinal thrombosis, which leads to destruction of retinal tissue by hæmorrhagic extravasation, and which is also associated with blood vascular degenerative changes; treatment in this state also is of little avail.

3. There is, however, the third type which I am confident should be isolated as definite clinical entity, and for which I suggested the name of retinal petechiasis. (1) The clinical history and definite ophthalmological appearances; (2) the prognosis; and (3) the response to treatment of retinal petechiasis are all three sharply defined from those of retinal hæmorrhage.

The difference between the clinical history of retinal petechiasis and that of hæmorrhage is striking. My experience shows that the high blood pressure which accompanies retinal hæmorrhage is not a factor in retinal petechiasis. Retinal petechiasis may occur at any time from middle age onwards. The youngest patient in my series was a female aged 40 years, and it may occur in advanced age. The age of a patient should be no deterrent to investigation and treatment. Two of my cases amply illustrate this important point. The age of the one was 80 and the age of the other was 83, the former patient after treatment, but not before, was able to read the type of an ordinary novel, and the vision of the latter improved to 6/12 part and Sn. 4. Both these patients were referred to me by their ophthalmic surgeons as having very poor vision. Again, in retinal hæmorrhage there are signs elsewhere of vascular degeneration, but in petechiasis there may be no such evidence. The urine in my cases of retinal petechiasis, with one exception, showed no abnormality, and there was no case where polyuria was a symptom.

Pathology.

From a pathological view it is not a true retinal hæmorrhage, but differs from it in several important respects. In retinal petechiasis the blood-vessel wall is not ruptured and blood is only exuded from a vessel with intact walls. This is well seen in the coloured plate (Figs. 1, 2, 3) where intact blood-vessels can be seen traversing the exudate.

The distinction I make between retinal petechiasis and retinal hæmorrhage may be compared to the rusty sputum of pneumonia and to the hæmaturia in

acute nephritis. Although blood appears in the sputum and urine, respectively, it has escaped from the blood-vessels by exudation and not by rupture of the walls. When walking along the banks of a brimming stream one can often notice little patches of well-grown grass in ground so sodden with moisture that water oozes out with the pressure of every footstep. The stream has not burst its banks; its water has exuded into the neighbouring soil.

Retinal petechiasis is produced in an analogous way. There is an exudation of blood without rupture of a blood-vessel, and it is a process that has quite a different pathology and significance to retinal hæmorrhage that is a result of rupture of a blood-vessel wall. It is impossible to speak dogmatically of the pathology of retinal petechiasis because so far as I know no opportunity for pathological examination has been possible other than that afforded by ophthalmoscopic means, which show definite and characteristic appearances.

In a well-marked case the retina appears bespattered with blood-stained mud (see Figs. 1 and 2). In severe cases these splashes may be confluent and the vitreous may be cloudy. The appearance then looks as if it were a true hæmorrhage. In severe and mild cases alike, however, these splashes have no relationship to ruptured blood-vessels, and in Figs. 2 and 3 intact blood-vessels may be seen to traverse the exudation.

Keogh, of Copenhagen, has shown that "when the capillary walls are subjected to stimulation the response may be in the nature of a contraction or relaxation, and also that with relaxation they may become increasingly permeable to the constituents of the blood plasma until when fully dilated they fail altogether to retain them. Toxins circulating in the blood can act as stimulus to produce this relaxation." It is my belief that splashes in retinal petechiasis are produced in this way. That similar lesions may occur elsewhere in the body from a similar causation is a necessary corollary, and this matter will be discussed later.

If the assumption is correct that retinal petechiasis can be produced in this way one should be able: first, to discover sources of infection; second, one should be able to remedy retinal petechiasis by the removal of these sources; third, a recurrence of the septic trouble should give rise to fresh manifestations in the retina; and fourth, similar lesions which can be seen elsewhere than in the retina and where direct visibility is also possible, the urinary bladder for example, these should also be subject to the above conditions.

Clinical Conditions.

I will now proceed to adduce clinical instances which fulfil these conditions.

(1) *Sources of Infection.*—Fifteen cases have been reported by me in full and in all of them a definite focus of infection was discovered, and in some two or more foci were detected. Concerning the site of these focal infections the teeth, the tonsils, the accessory sinuses of the nasal cavities, the ethmoid, and the urinary tract have been discovered in my cases, either respectively or collectively to be responsible for retinal petechiasis.

Good and rapid results have followed the removal of focal sepsis. Infected teeth were extracted, septic tonsils enucleated, and sinuses treated. In those cases in which operation was contraindicated, as in sepsis of the urinary tract, vaccines were employed and medicines were given, and the results were eminently satisfactory.

(2) Out of the 15 cases marked *improvement in vision* rapidly followed treatment in 10, moderate improvement in 2, no improvement with relapse in 2, and 1 case was not seen again. In the case in which improvement was marked the cloudy vitreous became clear very rapidly and within a week there was in most cases a marked improvement in vision, the best improvement being 6/60 to 6/6 and Sn. 14 to Sn. 1. (It has been suggested that the early rapid improvement is due to the disappearance of œdema in the macular region.) It will be agreed that this answers the second condition that the removal of the septic focus arrests petechiasis in the retina.

(3) *Recurrence.*—The recurrence of splashes in the retina resulting from the recurrence of the original septic trouble is, perhaps, the best proof of my contention. In three cases I can supply this necessary evidence. In one of them fresh splashes in the retina occurred with a marked deterioration in vision, after an exacerbation of ethmoidal sepsis of long standing and improvement resulted again immediately the sepsis was treated.

In the second case, one of tooth sepsis, a recurrence of failing vision led to the re-examination of the patient and the left tonsil was found to be very septic, although throat specialists had formerly passed both tonsils as normal. It was impossible to operate in this case; the tonsil was, therefore, treated locally and a vaccine was also administered. The improvement was not to the extent one would have hoped, but it was quite definite. The third case was first referred to me six years previously for "hæmorrhage" in the right eye and deterioration of vision to 6/60. On examination at that time I failed to detect buried tonsils, as it was not my custom then to retract the anterior pillar of the fauces in order to make a proper examination. She returned six months ago with hæmorrhage in the left eye, and then I found by retracting the pillars very septic buried tonsils. The vision in this eye was down to 6/60 and the vitreous was cloudy. The tonsils were enucleated at once and in four weeks the vision in the left eye was 6/6 c. glasses. She returned again four months later and the vision again was down to 6/60 and the vitreous was again cloudy. A careful search was again made for sepsis. No focus was found but a catheter specimen taken by myself with extreme caution showed at the end of 24 hours a heavy growth of streptococcus in pure culture in the urine. This case is now under treatment, and has already shown marked improvement. These recurrences are distressing but serve to prove my contention, and they point to the advisability of keeping a watchful eye on cases supposed to be cured.

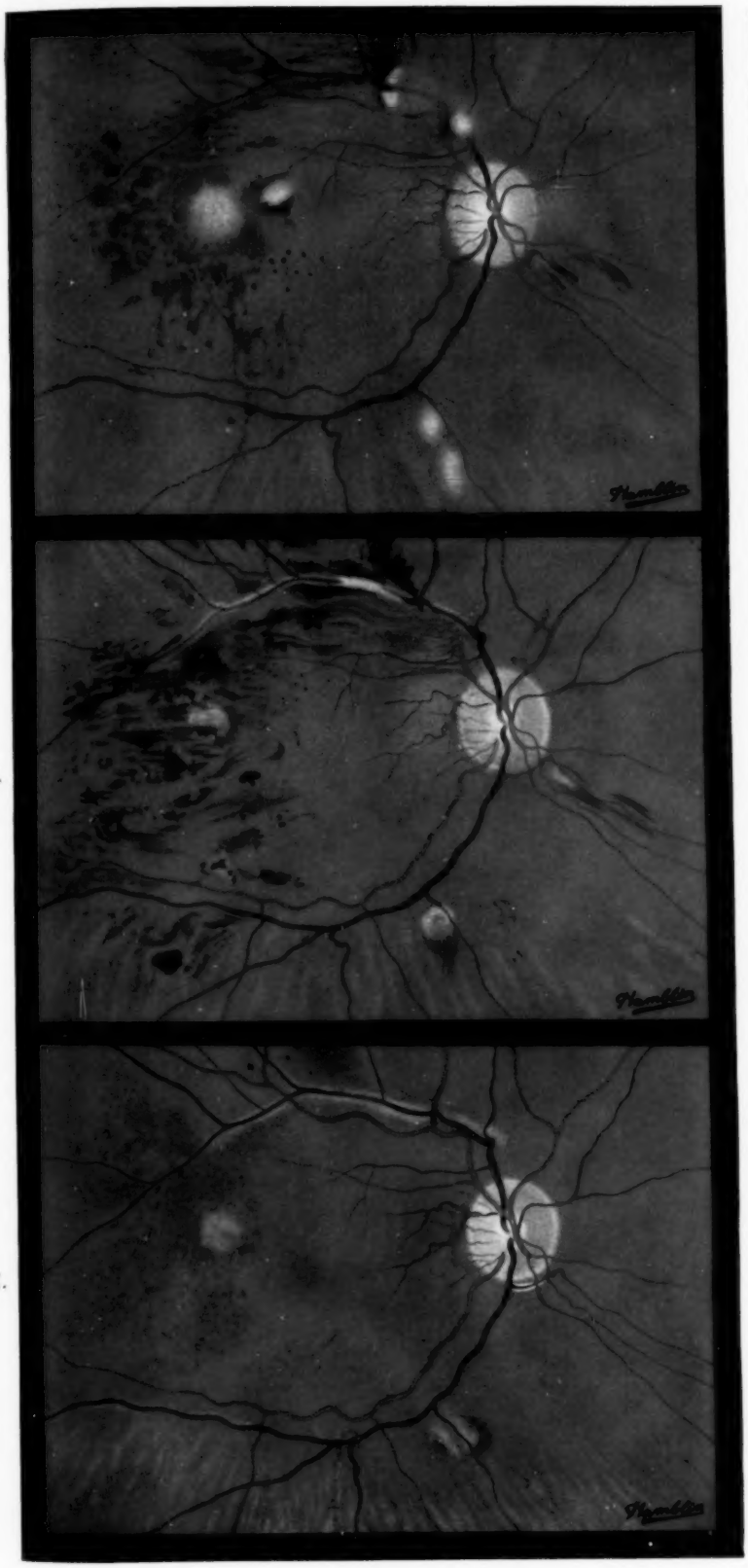
(4) *Similar lesions* elsewhere in the body. I am not in a position to supply evidence in support of the fourth condition—namely, that similar states should be found elsewhere in the body as a result of similar pathological conditions. However, Kidd has found and reported on a case of a similar state in the bladder to which reference will later be made.

I have said enough to prove that retinal petechiasis is an important clinical entity which should occupy a position of its own and should not be classified any longer under the heading of retinal hæmorrhage. The reason prompting me to prove that retinal petechiasis is a clinical entity is that in my opinion a type of blindness due to this pathological condition exists and is curable, but so long as it remains amongst the group of hæmorrhages of the retina it must unfortunately remain amongst the class of incurables.

THE POSSIBILITY OF A HÆMORRHAGIC STATE ELSEWHERE BEING A CONDITION SIMILAR TO RETINAL PETECHIASIS.

While writing this paper concerning petechiasis as it appears in the retina I was aware that it may also be occurring at the same time, either with or without retinal changes, in other internal or external surfaces of the body, and that the retinal changes might be only a local expression of a state of affairs which probably had a wider distribution.

There is no doubt that the careful study of this state opens up an entirely new vista and leads one into a new realm of possibilities in diagnosis and treatment of certain states elsewhere in the body where hæmorrhage occurs. Kidd touched on the subject as far back as 1913 in a contribution to the *Annals of Surgery* entitled Purpura of the Bladder. The case described by him was one of hæmaturia, which he considered was due to purpura of the bladder, secondary



I.

II.

III.

THESE figures illustrate a typical case of retinal petechiasis.

The patient was a man, aged 49, who a month previously had suddenly lost the sight of the right eye. The case was referred to me with the report of a hæmorrhage in the region of the macula of the right eye with a cloudy vitreous vision 6/60. My general examination showed a normal cardiovascular system, a B.P. 148–86, no albumin or polyuria, a very septic mouth with pus from two stumps of lower wisdoms which had been left two years ago after an attempt at their extraction had been abandoned. There was also a very septic but intact upper left molar and two very septic tonsils.

FIG. I. is an exact drawing of the state of the retina at this time. Note (1) the exudates in the region of the macula and due south of the disc, (2) the vessels running north-west of the disc passing through the exudate, and (3) the linear splashes due east of the disc.

The teeth were at once extracted.

FIG. II. depicts the same area three weeks later; fresh splashes had occurred, although the vision had improved to 6/36. It was then decided to enucleate the tonsils. Three weeks after this operation was performed the vitreous was clear, the splashes had almost entirely disappeared, and vision was 6/9 Sn. 4.

FIG. III. depicts the same area nearly two months after enucleation of the tonsils. The vitreous was clear and vision 6/6 and Sn. 1.c. glasses. The exudate has almost completely disappeared.

In comparing the states of blood-vessels in Figs. I., II., and III., the vessels can be seen passing through the exudate blood. In Fig. III. the vessel wall is intact, although there is still some exudate around it, showing that the vessel has not ruptured.

DR. H. MORELAND McCREA: RETINAL PETECHIASIS.

to a bacterial infection of the tonsil. The appearance of the bladder by cystoscopic examination, while the hæmaturia persisted, he described as follows:—

"The bladder wall for the greater part appeared pale and healthy, but scattered irregularly over fundus and trigone were seen patches of submucous hæmorrhages varying in size from a pin's head to a sixpence. The patches were of all shapes and sizes, some linear, some stellate. The greater number were scattered over the fundus. There was no ulceration."

A fortnight later, after the hæmaturia had ceased, cystoscopic examination revealed no evidence of hæmorrhage in the mucous membrane of the bladder. There is a striking similarity in the appearances at the first examination of the bladder to those described by me in the retina (see Figs. 1, 2). The similarity of their disappearance is also complete. The fact that Kidd has found a state in the bladder similar to that I have described in the retina and that he considers it to be due to a precisely similar cause—namely, a septic focus elsewhere in the body—opens up an important field of inquiry. Here are two situations in the body where it is possible to observe vessels and to watch their pathological changes and in both places petechiasis has been described by different observers, causing in one the splashes in the retina associated with cloudiness in the vitreous and in the other a similar lesion in the bladder mucosa with hæmaturia.

I believe it is true that the retinal changes I have described and also the changes in the bladder described by Kidd are due to the presence of a septic focus elsewhere in the body. If this be so, then the larger proposition is also highly probable, that many hæmorrhages from other mucous membranes of the body may also be due to petechiasis from the same causes—namely, septic foci elsewhere in the body. For example, not infrequently operations are performed on the abdomen for hæmatemesis or melæna in the belief that ulcers of the stomach or duodenum will be demonstrated, yet none have been discovered.

Two cases occurring in my own experience illustrate this point. They had symptoms of duodenal trouble with melæna. In the first, at the operation small petechial hæmorrhages were visible in the second part of the duodenum without definite evidence of ulceration; in the second, a similar state was found by the surgeon who was satisfied there was also a thickening in the first part of the duodenum which he considered to be an ulcer. Some time later old chronic septic antra in the first case and very septic tonsils in the second were dealt with. They are now quite well, but the cure of their digestive trouble was completed only after the removal of the septic foci. If septic foci had been discovered and treated earlier in these cases the hæmorrhages might have been cured without the performance of abdominal operations.

Further, it is conceivable that blood corpuscles which have exuded from a capillary may be so great in proportion that they may rupture the continuity of an epithelial surface or render its nutrition so feeble that gastric duodenal or intestinal secretions may act upon it and produce ulceration. Therefore my observations in the retina in conjunction with Kidd's observations on the bladder bear upon gastric duodenal and intestinal dystrophies in the two following remarkable ways.

(1) Hæmatemesis and melæna may be caused simply by petechiasis in the mucous membrane of these parts due to septic foci elsewhere in the body.

(2) Petechiasis may end in actual ulceration in the stomach, duodenum, and intestine. Consequently it is of the utmost importance in any of the above events to seek and cure a septic focus before excising or operating upon viscera in cases of hæmatemesis, melæna, or hæmaturia. Further, it is possible that metrorrhagia or menorrhagia may again be examples of petechiasis due to a septic focus elsewhere in the body.

THE ALLERGEN-PROOF CHAMBER
IN THE TREATMENT OF BRONCHIAL ASTHMA AND OTHER RESPIRATORY DISEASES.

BY W. STORM VAN LEEUWEN,
W. EINTHOVEN, JUN., AND W. KREMER.

(From the Pharmaco-Therapeutic Institute of the University of Leiden, Holland.)

IT is generally acknowledged that almost all cases of bronchial asthma and urticaria belong to the so-called allergic group of diseases; that is to say, the attacks are caused by inhalation or ingestion of substances called allergens—e.g., horse-dandruff and other so-called animal proteins, various pollens, and particular kinds of food. If the causal agent of the attacks is known, specific therapy may be applied by injection of small quantities of solutions of the allergen. In many cases, however, it is impossible to implicate one particular allergen as the causal agent, and non-specific treatment has therefore to be tried.

In an article published in THE LANCET in 1921 [1] it was suggested that in allergic diseases the use of tuberculin was the most valuable form of non-specific treatment. We have now treated over 500 cases by this method, and our results are as follows: cured, 50 per cent.; improved, 30 per cent.; failures, 20 per cent. These results are valuable, but not satisfactory; it is noteworthy that nearly all investigators who publish statistics on the treatment of allergic diseases estimate their failures at about 20 per cent.

Work done during 1923 and 1924 [2] showed us that our failure to achieve more than 50 per cent. of complete cures was almost entirely due to the fact that factors of climate played such an important part in these cases. We realised that if it were possible to bring all these patients to a high mountain climate and keep them there permanently the problem of treatment would be practically solved. Other investigations showed us that the influence of a high mountain climate on allergics is almost entirely due to the relative absence of allergens in the atmosphere. The allergens occurring in the air of lower countries we called *climatic allergens*.

Since it is impossible to send all asthmatics to high altitudes and keep them there we considered the possibility of making such arrangements in patients' homes that they should be free there from contact with climatic allergens. This problem has been studied during the last two years, and we can now state that it has been practically solved. Allergen-proof rooms are now used by a number of patients in our country. The system worked out by us is so simple and gives such good results that it will probably open up new ways of treating allergic and other diseases. Of course this does not mean that the older methods of anti-allergic treatment—including the use of tuberculin—have become useless; on the contrary, they are still of great importance as additional measures. But in pure cases of climatic allergy the allergen-proof chamber has become the principal means of treatment.

Two Groups of Climatic Allergens.

Before describing the new therapeutic method we must first refer to a point which formerly puzzled us considerably, but proved to be a useful starting-point for further work. Every physician knows that many asthmatics are better in some places and worse in others, and also that many patients are free from attacks of asthma as soon as they are taken into hospital, even if the hospital is in the very town in which they live. The improvement which takes place at the hospital is not due to food, rest, or drugs, for

[1] W. S. van Leeuwen and H. Varekamp: On the Tuberculin Treatment of Bronchial Asthma and Hay Fever, THE LANCET, 1921, ii., 1366.
[2] W. S. van Leeuwen, Proc. Roy. Soc. of Med. (Sect. Therap. and Pharm.), 1924, xvii. 19.

it occurs if the patient is out of bed all day, goes home, and does his work—provided only that he *sleeps* at the hospital.

We have come to the conclusion that two kinds of climate-allergens must be distinguished. Probably it will be shown in a few years that allergens of these two groups are of a common nature, but for the present we draw a line between two groups, which we call A and B. Group A contains allergens which occur in the outside air; for example, the presence of such allergens in Bristol may induce attacks in a man who is free from asthma in London. The nature of allergens of Group A is unknown, although we have been able to prove their existence beyond any doubt. Group B contains allergens which occur and are formed in private houses. They are absent, or almost absent, in well-organised hospitals. Various workers have found examples of such allergens—e.g., house dust, grain contaminated with small insects (mites), unknown substances in certain feathers used in pillows, bedding infected—as often happens in private houses, but seldom in hospitals—with fungi, especially *Aspergillus fumigatus*.

Most patients are very sensitive to allergens of Group B, and they are practically free from attacks if protected from them. Protection may be obtained by building in their bedroom a small airtight chamber (Type I.) described below. A small number of patients are also sensitive to allergens of Group A to such an extent that the chamber of Type I., which only excludes allergens of Group B, is not sufficient; they must be put into a chamber of Type II.

Description of the Chambers.

By Prof. VAN LEEUWEN and Mr. EINTHOVEN.

TYPE I. is an airtight chamber, built of iron or any other material on which bacteria or moulds cannot grow. The room must be small—$6 \times 6 \times 9$ ft. suffices. In the front wall of the chamber is a door which shuts tightly; in one of the side walls is a large window, to face the window of the room in which the chamber is to be placed. The walls are painted and varnished, so that they may be easily cleaned.

The chamber contains an iron bed and an iron chair. Mattresses, pillows, and other bedding are ordered fresh from the shop; they are sterilised before entering the chamber and again every two months. Before going to bed the patient undresses in his bedroom and then enters the chamber and shuts the door at once; he stays in the chamber during the whole night and he does not take into it any clothes, extra pillows, books, or food. The chamber is ventilated by an exhauster which blows in 70 cubic feet of air per minute. In one of the side walls is a hole to let the air escape; this hole is connected with an outlet. For most purposes it is sufficient if the exhauster draws in air by an iron tube protruding about 30 feet above the roof of the house; in winter, of course, the air must be heated before it enters, and this is easily done by putting some heating system in one of the tubes. If zinc tubes are used they must be varnished to avoid the possibility of dust of zinc oxide entering the chamber.

TYPE II.—The construction of this chamber is the same as of Type I. The only difference lies in the methods of purifying the outside air before it enters the chamber. Those suggested are as follows:—

A. *Refrigerator System.*—Early in our endeavours to obtain air free from allergens we tried to get rid of the "dust" in the air by means of moisture, and we devised several schemes for the purpose. We later found that they were all based on a wrong principle. One of the few things we know of the nature of allergens is that they are present in colloidal form and are very easily soluble in water, so that moistening the air or filtering it through moist tissue will never be satisfactory. In moist air these water-soluble colloidal particles will always be surrounded by some molecules of water. The proper method of getting rid of allergens is to make the air dry by cooling; the water of condensation will then contain a great part of the colloidal material which was previously present in the air. Thus the air can be effectively purified by being passed over the cooled surface of a refrigerator before entering the chamber. In the clinic for allergic diseases at Leiden there is a refrigerator with a capacity of 4000 calories per hour and a cooling surface of 180 sq. ft. This will reduce the dew-point of the outside air by 20° F. if about 150 cubic feet of air pass per minute, which suffices to ventilate two chambers of Type II. for two patients each. The cooled air has to be heated by means of a small central heating system. For the most part we obtain a relative humidity of 20 per cent. in our chambers, with a room temperature of 65°–70° F., which may be considered sufficient.

B. *Filters.*—One of our first projects was to purify the outside air by means of a filter. Cotton filters, which we used at the beginning, proved useless. Aided by the kindness of Prof. Gray, of Leeds, we tried various other materials, and at last found common asbestos paper to be the most satisfactory. We have constructed asbestos filters which have a capacity of 180 cubic feet per minute at a pressure of 25 cm. water. This pressure may be produced by an ordinary exhauster driven by an electric motor. Since this filter keeps back tobacco smoke entirely it may be surmised that all colloidal particles of a diameter above 10 $\mu\mu$ are taken away from the outside air. It has not been possible so far, however, to put this system on a sound financial basis. If a filter has only to free the air from pollen it is unnecessary to use asbestos paper, simpler filters of specially prepared paper being sufficient. They offer very little resistance and in practice they are found useful.

C. *Electrical Process.*—During discussion of the problem of dust-free rooms Prof. F. G. Donnan about three years ago suggested to one of us that we should use the Cottrell process. This is based on the following principles:—

In the centre of an iron tube (which is connected with the earth) a thin metal thread is placed. This thread is connected with a high voltage transformer and rectifier, so that the thread can be charged with about 50,000 volts. If air loaded with dust passes through the tube all the dust is thrown to the side of the tube; the air leaves the tube purified.

This method has, for clinical purposes, the great drawback that the air leaving the tube contains so much ozone that it cannot be breathed. We had to find a device for getting rid of the ozone. Dr. Nijk succeeded therein by the use of mixtures of various metallic oxides, but this system also, it was found, could not be put on a reasonable economic foundation.

Clinical Results.

By Prof. VAN LEEUWEN and Dr. W. KREMER.

More than two years ago a special clinic for the treatment of allergic diseases, based on the principles laid down in the preceding section, was arranged in Leiden. For this purpose two private houses were rented; they were damp and rather badly built, and were situated on clay soil in a very moist part of the city. In eight rooms of these houses small allergen-free chambers were built and arrangements were made to enable us to ventilate each chamber with outside air or purified outside air.

So far about 500 asthmatics have been admitted. Of these, about 75 per cent. became free from asthmatic symptoms within two or three days; about 15 per cent. were distinctly improved after two or three weeks, and 10 per cent. remain uninfluenced. Some years ago K. Turban and L. Spengler, in an account of the influence of high mountain air on asthma, stated that at Davos 68 per cent. of asthmatics became free from symptoms within two or three days; 25 per cent. were much relieved after two or three weeks, and 7 per cent. remained unchanged. It is clear, then, that our results are the same as those of the Swiss authors, which affords undeniable evidence for the correctness of our view that the beneficial influence of high altitude on asthma is due to the lack of climatic

allergens. Furthermore, our observations proved that conditions similar to those in high mountain air may be produced by artificial means in Holland or any other country. In this connexion it is noteworthy that our clinic is situated on clay soil in a moist region, which is naturally considered bad for asthmatics.

Of course those patients who improved during residence in the clinic were not cured of their asthma. As a matter of fact, most of them had attacks again as soon as they went home. In this respect, too, the effect of the allergen-proof chamber is similar to the effect of high mountain air. This being so, it may be asked why we took these patients into the clinic at all. It was done, first, to make a correct diagnosis and to observe whether the case was a "pure" case of climatic asthma; secondly, to determine whether other sensitisations—to products of animal skin or foodstuffs—were present; and, thirdly, to start anti-allergic treatment with small doses of extract of climatic allergens and to determine the efficient dose for treatment. Apart from this, admission to the clinic is of great value, since we can advise those patients who belong to the 75 per cent. of purely climatic cases to build an allergen-proof chamber in their own homes; or, if this is financially impossible, we may at least instruct them how to change conditions at home by looking after furniture, mattresses, blankets, and the like.

Allergen-proof chambers have been installed by a Dutch and a German firm in 45 private houses and have in almost all cases given complete satisfaction. The application of the system to private houses is possible as there are two favourable circumstances which have to be mentioned. First, it has turned out that climatic allergens of Type A—i.e., allergens occurring in the outside air—are of much less importance than those which occur and are formed in the houses, and consequently the simple type of allergen-free chamber is for the most part sufficient, very few patients needing the much more complicated and expensive type which arranges for purification of outside air. Secondly, it has proved that even patients highly sensitive to climatic allergens can stand a certain amount of allergen, so that it is not necessary for them to stay in their allergen-proof chamber day and night, and it suffices if they sleep in their chamber and stay in it some hours daily. In the daytime they may go out and attend to their work. Of course, there are some exceptions in which the cause of asthma is to be found precisely in the place where the work is done, but by this method we have been able to treat successfully cases which have absolutely resisted all other forms of treatment. It goes without saying that for safety's sake we give anti-allergic treatment also to those patients who have a chamber at home and try to desensitise them gradually with injections of small amounts of climatic allergens.

Whooping-cough and Tuberculosis.

Recently we have applied the principle of treatment in allergen-proof chamber to two other illnesses—whooping-cough and tuberculosis. Only five cases of whooping-cough have been treated, but the results were so striking as to justify publication, the more so as probably we will not be able to extend our observations in this direction in the near future. All our whooping-cough cases came into the clinic during or before the height of the illness; they had violent attacks at least every two hours. These violent attacks ceased from the moment they entered the allergen-proof chamber (ventilated with purified air). We did not notice any severe attack with cyanosis, although some attacks, eight at most of a very mild degree of severity, occurred during the first few days. After four to seven days the children were free from cough. We do not know the explanation of this sudden improvement, but simply report the facts as they may be of theoretical and practical interest.

Sixteen patients with tuberculosis of the lungs were admitted to the clinic and kept in allergen-proof chambers. They were pure cases of severe tuberculosis with symptoms and clinical signs of the disease confirmed by radiographic examinations. In the seven who had sputum examination showed numerous tubercle bacilli. Three patients remained uninfluenced by residence in the allergen-proof chamber, but all the others improved. In two very severe cases the improvement was only temporary; they could not be saved and died after half a year and a year. Improvement was shown very soon after admission to the clinic and consisted of: more ease in breathing, much less coughing, improvement in appetite, increase in weight (3 to 15 kg.), lowering of bodily temperature, and in some cases reduction in the amount of sputum. In three cases with distinct cavities the reduction in the amount of sputum was very marked. The ultimate results of the treatment of pulmonary tuberculosis in allergen-proof chambers cannot yet be judged. We only want to emphasise that the first result of admission to allergen-free air in 13 out of 16 cases of severe tuberculosis of the lungs was a distinct improvement; so that the conclusion is permissible that also in this respect the advantage of high mountain air may be obtained in low countries by artificial means. The lack of ultra-violet rays in our allergen-proof chambers may, of course, easily be made good by the use of quartz lamps.

Clinical and Laboratory Notes.

FOUR CASES OF TETANUS FOLLOWING INTRAMUSCULAR INJECTION OF QUININE.

BY JOHN MACQUEEN, M.B., CH.B. EDIN.,
SENIOR MEDICAL OFFICER, DEPT. OF HEALTH, PALESTINE.

IN September and December, 1925, four persons died in Haifa from tetanus following intramuscular injection of a solution of quinine bihydrochloride into the buttocks. They were all adult males. The following are notes of the cases:—

CASE 1.—The patient received injections of 1 g. quinine bihydrochloride on Sept. 15th and 16th. On the same day five other patients had injections of the same solution; two of them were alive and well in January, 1926, and the other three had gone to Transjordania and could not be traced. After the injections the patient received dental treatment and suffered from bleeding piles. Symptoms of tetanus set in about Sept 27th, 11–12 days after the last injection, and the patient died on Sept. 30th. No wound was discovered.

CASE 2.—Injections of 1 g. were given on Nov. 3rd, 4th, and 5th. Symptoms began about 28 days later, and the patient died after an illness of 2–3 days on Dec. 5th. He died out of hospital, but so far as is known there was no wound except that of the injection.

CASE 3.—The symptoms came on 28 days after the last of three injections on Nov. 4th, 5th, and 6th. The illness lasted 24 hours and the patient died in hospital. There was a history of an ingrowing toe-nail which he used to pare. No wound was discovered. Between Nov. 3rd and 6th two other patients received injections (also of 1 g.), with the same series of needles (reboiled) and with the same quinine solution, possibly from a different bottle. Both were alive and well in January, 1926.

CASE 4.—The fourth patient received his injections on Nov. 11th, 12th, and 13th. Definite symptoms of tetanus were first noted on Dec. 4th, 21 days after quinine was last given, and the patient died in hospital on Dec. 7th. No wound other than that of the injection could be discovered. Between Nov. 6th and 13th nine other patients were given injections from the same solution. All were alive and well, so far as we knew, in January, 1926; most of them were seen.

The quinine solution for the injections in September (Case 1) was prepared before Sept. 5th. That used during November was made up during October.

Method of Preparation.—Vaccine bottles (25 c.cm.) are well washed and rinsed with alcohol. The quantity of quinine bihydrochloride required is measured out and placed in a glass measure and distilled water is added to make a 50 per cent. solution. The solution is filtered and poured into several vaccine bottles. These are rubber-capped and sterilised in an autoclave at 15 lb. and 120° C. for half an hour. They are stored in a poison cupboard and a new lot is prepared about every six weeks.

Before use the rubber cap is dipped in iodine. The needle pierces the cap.

Technique of Injection.—Injection is made into the gluteal muscles on the outer part of the buttocks. The skin is prepared with 3 per cent. tincture of iodine. Two or three needles are boiled and reboiled between each injection. Boiling of syringe and needles is for 15 minutes in the first instance. After injection hot fomentations are used.

There are certain points of interest in connexion with these cases. The incubation periods were long: in two cases 27 to 28 days, in one 21, and in one 11–12. The illnesses, on the other hand, were unusually severe. The time between onset of symptoms and death was in no case more than 72 hours.

The conclusion was reached that the infecting spores were in all four cases introduced at injection. There did not appear to have been any obvious defect in the manner of preparation of the skin, the technique of injection, the sterilisation of syringe and needles, or the preparation and sterilisation of the solution. Similar methods had been employed for a considerable time and were used in military hospitals during the war. The cases remind us that quinine solution causes necrosis of muscle-tissue and that necrosed tissue shut off in this way from the air may form an ideal nursery for tetanus spores if they happen to gain entrance. It is not easy to maintain a technique which will exclude all possibility of introducing them. They provide a further argument in favour of the oral as compared with the intramuscular route for the administration of quinine whenever possible.

The subject is dealt with by Sir D. Semple in Memoir No. 43 (New Series) of the Series of Scientific Memoirs by Officers of the Medical and Sanitary Departments of the Government of India, published at the Government Printing Press, Calcutta, in 1911, and entitled "The Relation of Tetanus to the Hypodermic or Intramuscular Injection of Quinine."

A CASE OF AURICULAR FIBRILLATION OF FIFTEEN YEARS' DURATION.

BY E. E. LASLETT, B.SC. LOND., M.D. MANCH.

THE following case seems worthy of record.

Mrs. K. first came under my care in July, 1910. She was then 48 and had five children. She had had rheumatic fever 20 years before, but had enjoyed fairly good health since. She complained of breathlessness and swelling of the feet. The apex beat could not be defined. There was a systolic murmur at the mitral area, and the rhythm was irregular owing to the presence of frequent auricular extrasystoles.

In January, 1911, she became much worse. The dropsy increased, orthopnœa was present, and the pulse became very rapid and wholly irregular. It was found that the venous pulse was now of the ventricular type (auricular fibrillation). The heart slowed in a few days under ℥ xlv. tinct. digitalis daily and there was general improvement in her condition. A faint diastolic murmur could now be heard at the left side of the lower end of the sternum. The improvement continued till April, when the more serious symptoms returned. There was again a rapid response to treatment and the pulse fell to 40 with a tendency to coupled beats. The dose of digitalis was now halved and kept at this amount for some time.

During the next ten years she was able to do her own housework for the most part, although in the latter part of this period attacks of bronchitis became more frequent and prolonged. She was kept almost continuously under the influence of digitalis. Œdema of the feet was often present to a slight degree, but it disappeared during her periodic rests in bed. In the winter of 1920–21 she was very ill with increased dropsy, cyanosis, and enlargement of the liver. In the following winter she was in bed for several months, and from that time till her death she was kept almost entirely in her bedroom. As a result of the increased rest, and, probably also owing to the development of partial block, the heart tended to a slower rate, so that it was found possible to reduce the amount of digitalis to ℥ xxiv. and even ℥ xv. daily.

In April, 1922, she had an attack of aphasia, possibly embolic in origin. This passed off in a few days, and her mental condition became apparently normal. On the whole she had little physical distress. Though she chafed at her enforced rest she was able to amuse herself with reading and light feminine occupations, and she was probably in greater comfort than she had been for a number of years. At the end of 1926 she was sitting up in bed apparently as well as usual when she suddenly fell back unconscious and died in a few hours.

Dr. John Cowan, in his Gibson lectures,[1] relates a case in which fibrillation was known to exist for nearly 12 years. Four years after the onset of fibrillation the patient had her sixth child. She died at the age of 39. In the case here recorded fibrillation was present for 15 years, and this in spite of the fact that at the time of its onset the patient was nearly 50 years of age and showed signs of a failing heart. One is tempted to suggest that this change of rhythm, although it is so often an added embarrassment to a damaged heart, may have been helpful rather than injurious to this patient, because her heart responded so readily to digitalis and she was fortunately able to continue treatment during the whole of her illness.

Hull.

A NOTE ON EPILATION BY THALLIUM ACETATE.*

BY F. R. CURTIS, M.SC., M.B., CH.B. LEEDS,
KING'S COLLEGE, STRAND.

As the result of experiments begun by A. Buschke in 1900 and carried on by himself and others,[2] it has gradually been established that thallium acetate, which 30 years ago had been given up as dangerous by Sabouraud, can safely be used for epilation in cases of ringworm in young children as an alternative to X ray epilation which, as is well known, possesses disadvantages in these cases. Early this year G. B. Dowling and R. Kelman,[3] and M. Drummond,[4] reported the results of using this method for epilation in children suffering from ringworm. Both these reports suggested that the preparation of thallium should be fresh, because the drug might deteriorate. As this supposed deterioration is a matter of considerable importance it was thought advisable to investigate it.

Using rats as experimental animals I find that epilation occurs constantly on the seventh or eighth day after the subcutaneous injection of a solution of thallium acetate equivalent to 7·5 mg. per kilogramme of body-weight. In all cases the solution was freshly made immediately prior to injection. The best site for demonstrating epilation at that period after injection is, as Dixon[5] points out, at the back of the head and neck and just behind the ears.

Solutions of thallium acetate, prepared and placed in sterilised ampoules three months previously, were tested on a series of rats using the dose given above. Epilation occurred promptly on the eighth day after injection, thus showing that the date of the preparation is not of any moment.

Another point that may be worthy of mention is the danger of giving a second dose too soon after the first dose. Rats may be given a dose of 22·5 mg. per kg. of body-weight subcutaneously and remain perfectly healthy in every way, though, of course, epilation occurs freely. But if 7·5 mg. per kg. is given and then three weeks later a further 15 mg. per kg. is given (making the same total of 22·5 mg. per kg.) the rats die within a few days, having shown loss of appetite and weight, conjunctivitis, stomatitis, and epistaxis. This cumulative effect of thallium is very marked and Buschke advises not giving a second dose within two to three months of the first.

Experiments on the mode of operation of thallium are now being carried out at King's College and, it is hoped, may throw some light on the problem.

[1] Edin. Med. Jour., 1926, xxxiii., 550.

* This work has been carried out in collaboration with the Research Department of Messrs. May and Baker Ltd., Battersea, to whom I am indebted for the supplies of thallium acetate.

[2] Dermatologische Wochenschrift, August 3rd, 1926; and Urologic and Cutaneous Review, 1926, xxx., 449.

[3] THE LANCET, Feb. 19th, p. 389. [4] Ibid., Feb. 12th, p. 343.

[5] Dixon, W. H.: Proc. Roy. Soc. Med., June, 1927.

Medical Societies.

MEDICAL SOCIETY OF LONDON.

A GENERAL meeting and conversazione of this Society was held on June 13th, Sir HUMPHRY ROLLESTON, the President, in the chair. Following the business meeting, the annual oration was delivered by Prof. HARVEY CUSHING (Harvard University, U.S.A.).

The PRESIDENT, in a few introductory words, referred to the importance of Prof. Cushing's contributions to medical literature, and especially to his work on the surgery of the central nervous system. He was outstandingly fitted to the happy definition of the surgeon as a "physician who can use his hands," and he could use his pen with equal facility. Everyone must have been charmed by his Life of Sir William Osler, his teacher and friend.

Prof. HARVEY CUSHING took as the title of his oration

THE SURGICAL ASPECTS OF ACROMEGALY.

He said that though the medical man began his professional life with a general training he soon found that there were certain maladies or phenomena of disease which particularly interested him, and which, through force or opportunity or circumstance, engaged his attention. It was by progression from the general to the particular that specialisation arose, and though in the process the field might narrow, the point of view might broaden.

Those who could go back to the 'nineties would know that the pituitary body was then too inconspicuous an object to attract much attention; if noticed at all it was brushed aside as a vestigial relic of no recognisable importance. There were, however, glimmerings of its relationship to the disorder to which Pierre Marie had recently given a baptismal name. Once pointed out, this disorder was easily recognised, though for a time it was regarded as a freak of nature which eclipsed understanding, nothing then being known of the function of the pituitary body or of its relation to other glands having an internal secretion. How different the aspect now, when the problems of endocrinology were absorbing the attention of a host of investigators, who, almost monthly, were adding to knowledge on the subject.

There were certain general principles on which the profession had come to base its conception of the way in which the disorders of the ductless gland affected the body. The first of these arose from the presumption that there were counterposed states of primary under-function and of primary over-function for every single member of the so-called endocrine series. And it was assumed that these two states, in the case of every gland, would evoke their own peculiar clinical syndromes. Some of these, which were already recognised, and some—particularly the deprivation states like myxœdema, diabetes mellitus, eunochoidism, and tetany—could be experimentally produced in animals; the states of glandular over-activity had for the most part proved difficult to reproduce experimentally.

Surgery had played no small part in the elaboration of this theory. Enlargement of the thyroid was for all to see, and in localities where goitre was endemic the surgeon had primarily been induced to operate upon cases in which life was endangered or made insufferable owing to pressure by the enlarged gland on the trachea. These procedures had proved hazardous. It had then become evident that a residuum of thyroid tissue must be left, and that the parathyroid glands must be spared if subsequent health, and even life, was to be maintained. The pituitary problem, however, was far more difficult, and not until skiagraphy was sufficiently perfected to be reliable, had it been possible to tell with any certainty whether that gland was tumefied. Its inaccessibility had long kept it out of the way of surgical temptation, and even its experimental removal in animals was difficult and gave contradictory results, largely on account of coincident adjacent lesions of the nerve centres, which possibly presided over the activity of the neurohypophysis.

Function of the Pituitary Body.

One of the first questions to be raised in regard to acromegaly concerned its likely connexion with pituitary tumours. And at last investigators were coming to close quarters with the riddle. The physiologists and biochemists had chiefly given attention to the active substance discovered in extracts of the neurohypophysis, the pathologists had had some success in differentiating certain of the hyperplasias and other tumefactions affecting the gland; the morphologists had shown how, in the development of Rathke's pouch, the epithelial *anlage* of certain of the congenital tumours might arise; whilst the experimentalists had laboriously undertaken to determine the secondary effects of removing part or all of the gland.

Early experiments showed that the hypophysis secreted a substance or substances which not only influenced growth, but also had a marked effect upon the activity of the reproductive organs. Physiologists had discovered an active principle only in extracts of the posterior lobe of the gland, this principle being a stimulant to growth. Menstrual disturbances were common in women who had disease of the pituitary, whatever the nature of that disease might be. Prof. H. M. Evans had shown that fresh extracts of the anterior lobe would not only interrupt œstrus in an adult female rat, but would prevent its onset when it was given to pre-adolescent animals. The same worker had found that when intraperitoneal injections of these extracts were continued over a long time the growth of the animals concerned was greatly accelerated, and that gigantism could in this way be experimentally produced. T. J. Putnam had succeeded in doing this, and it had been shown that the pars anterior actually contained a growth-stimulating hormone. This important fact would doubtless stimulate the biochemist to search for the chemical principle. When this had been finally isolated, the treatment of clinical states of anterior pituitary lobe deficiency would be revolutionised. These experiments had not produced acromegaly, but only gigantism, though both these conditions could be ascribed to excessive secretion of the anterior lobe. Prof. P. E. Smith, of Leland Stanford University, had devised an operative procedure whereby hypophyseal or parahypophyseal lesions could be accurately made, with results which were far more dependable than any previously attained, and the possibilities of replacement therapy to atone for this glandular deprivation had been for the first time demonstrated.

Prof. Cushing had something to say in criticism of some of the terms in current use in relation to hypophyseal disease. Did cachexia hypophyseopriva, due to destruction of the gland, really exist? He suggested that such a term as macrosomia might replace acromegaly; it would permit of its reverse condition being spoken of as microsomia.

Effects of disordered pituitary function on organs other than the sexual ones had also been investigated. In autopsies on four cases of acromegaly, not only was there splanchomegaly but also hyperplasia of the thyroid and parathyroid. Owing to a careful study of the rat and its habits, an immense field had been opened up in relation to pituitary function. It was clear that this structure conducted an orchestra, and derived from it harmony or dysharmony, overtones or undertones, according to its physiological mood.

Hypopituitarism.

Clinical states occurred which suggested that the patient suffered a complete deprivation of pituitary substance. It was now occasionally possible to remove the pituitary gland apparently in its entirety, even in the adult. It had long been noted in the case of animals that young ones stood the procedure much better than did adults. If it was clear in a

given case that there was a tumour of the hypophysis, was the surgeon justified in removing the gland in its entirety? Or was it possible by such a procedure to inflict on the patient symptoms which might be worse than those it was sought to relieve—i.e., tumour symptoms? Cases had been seen in which the patient was suddenly seized with severe headache, became stuporose and comatose, with a markedly subnormal temperature, and died in the coma. Such a syndrome would be very puzzling to the pathologist unless he realised, and was alert to the possibility, that acute lesions in the pituitary body might provoke such a clinical picture.

Hypopituitarism was the reverse condition to acromegaly. The effects were different according to the period of life—whether the state occurred in pre-adolescence or in adult life. He showed a photograph of a young women, aged 28, a dwarf. At 8 years of age she had a very severe infection—its nature was not clear—and was unconscious for a long time. After recovering from that acute condition she scarcely grew at all for 10 years. At 28 years she was just over 4 feet in height and weighed only 75 lb. It was a case of primary deficiency of the anterior lobe of the pituitary lobe alone. She was sexually infantile, and had never acquired any secondary sexual characters, while the other ductless glands were atrophied.

Photographs were also shown of a case of early senility, the subject being a young woman. The open epiphyses of the fingers, shown by X rays, indicated that by appropriate substitution-therapy she could be given the usual adult womanly characters. These people with pituitary deficiency died of old age in their 'teens, and to relieve their condition recourse must be had to substitution-therapy. This was much more hopeful in these individuals than in cretins, for however much the cretin might be made to grow as a result of appropriate medication, he always remained a dull and mentally incapacitated person. The pituitary cases might even, as a result of treatment, become precocious.

CONDITIONS ASSOCIATED WITH TUMOUR.

Up to the present point, said Prof. Cushing, he had been speaking of non-tumour states. When the pituitary condition was associated with tumour there were many names applied to it. The case on which was based the term Fröhlich's syndrome was that of a boy, with a tumour of the gland, who was adipose and sexually indisposed. Almost always the cases which began with a tumour in childhood were those in which the swelling originated from a relic of Rathke's pouch. There might not be any actual enlargement of the sella, but compression was exerted on some portion of the gland. There might exist a combination of symptoms of insufficiency, and these symptoms would usually be much less clear than in the cases of pure anterior lobe deficiency due to the presence of infarcts. When the disease began in early life, its subjects were dwarfed, as the anterior lobe was compressed. When the disease did not show itself until adult life, stature was retained.

Prof. Cushing showed slides to illustrate the frontal approach to the sella with exposure of the chiasma. He was careful not to belittle the seriousness of the operation, especially as these tumours were very adherent, and there was the risk that the surgeon might destroy the hypophysis or its important blood-supply, thereby provoking serious secondary symptoms. In about 83 per cent. of the cases enlargement of the sella could be seen by careful skiagraphy. Patients might be either adipose or lean, according to the part of the gland affected.

He also dealt with hypopituitary cases associated with adenoma. This was a very important class of case, as pituitary disease which led to gigantism was invariably associated with adenoma. What ought the surgeon to do in cases with adenoma? In his own clinic there had now been two or three hundred of these cases which had been operated upon—adenomata of all types. He showed the photograph of a typical case. The man was blind in one eye, the other was afflicted with optic atrophy, he was adipose, and had sexual dystrophy. His adenoma was attacked sufficiently radically to relieve the pressure on the chiasma and to prevent vision from being lost altogether. But was that enough? Was the surgeon justified is going ahead and attempting more, thereby running the risk of setting up deficiency states?

The cases with adenoma he divided into the primary, the transitional, and those having an affinity for an acid diet. Some of the tumours in acromegaly were of enormous size. He showed a photograph of the site of a large tumour in the brain of a giant of 8 feet, in whom adenoma was not suspected, as he had no visual disturbance and did not complain of any intracranial symptoms. His sella turcica was seen by X rays to be small, yet he had this extensive intracranial adenoma. In the States the practice was growing to operate on these people before their acromegaly became very pronounced or serious secondaries were manifest. In the case of the first man on whom he operated for the condition, in 1909, he was struck by the great shrinkage of the tissues of the patient's hands. The tumour in his case was small and the immediate purpose of the operation was to attempt relief of the headaches. That result was achieved and 19 years later he was still living, but the acromegaly had steadily progressed notwithstanding. No doubt the relief of the headaches was brought about by freeing the hypophysis from exterior pressure. In another case, that of a woman, he had operated for the relief of intense headaches, and she was much better for three or four years. Then a radical operation was done by another surgeon (as Prof. Cushing was in Europe) and the gland was removed; now the original acromegaly had been transformed into a condition of relative pituitary insufficiency, a preferable state from the patient's standpoint.

The Criteria of Success.

In conclusion, Prof. Cushing said there did not yet exist a standard or criterion of what the surgeon or physician had accomplished in the kind of cases under discussion; there was nothing comparable to the basal metabolic rate by which the activity of the thyroid could be assessed. Still, progress was now being made in this direction. Most of these patients had a high metabolism. Was that due to the pituitary lesion or to the associated or secondary hyperplasia?

The crucial indication was what happened to the patient when his hypophysis was removed. Even a partial operation would diminish the metabolic rate. The latter, and the sugar tolerance, were likely to give the criterion of accomplishment, as in the case of thyroidectomy. These patients were very apt to have a relative hyperglycæmia; could this be dissipated by operation? Those were the lines along which work in the States was proceeding.

It was yet too soon to speak with any finality of the effects of operations in this region. Operations were, in practically all cases, done through the nose. Unless the contents of the sella were completely evacuated it was impossible to be certain that some remnants of adenomatous tissue had not been left behind, and these were at any time liable to revive and produce a repetition of the former symptoms. He contended that the fact that any improvement could be brought about, even though it might be only temporary, should be an encouragement to go on. He had no wish to belittle the complexity of the subject. How far it was safe for the surgeon to go, how near to total evacuation of the causal adenoma he might approach, only experience could show. Serious consequences would follow damage to the hyperthalamic centre. Trans-sphenoidal procedures from below were blind operations, with a risk of resultant rhinorrhœa and infection. The 4 per cent. operative risk which was the present figure in his clinic was a good one, he submitted. Where vision was impaired the attempt was made to relieve it, and the surgeon carefully felt his way. In several cases having a small sella operation had been done with the object of checking

acromegaly, apparently with success. When a proper and reliable system of substitution-therapy had been established probably the operative risk would be less.

He had made an effort, in this address, he said, to evolve some order out of chaos, and even if he had done no more than indicate the true latitude and longitude he would feel content.

Sir CHARLES BALLANCE proposed a cordial vote of thanks to Prof. Cushing for his address, recalling the time when, in 1892, he had met the orator, who had come to Queen-square National Hospital as a student. He said Prof. Cushing had energy and a scholarly mind, and he expressed his intense admiration for him as a man and as a worker in neurology, of which he was a master.

Sir STCLAIR THOMSON seconded the vote, and after it had been supported by the President it was carried enthusiastically by Fellows rising in their places.

ROYAL SOCIETY OF MEDICINE.

SECTIONS OF LARYNGOLOGY AND OTOLOGY.

THE annual summer meeting of these Sections was held from June 9th–11th, the Presidents, Dr. ANDREW WYLIE (Laryngology) and Dr. DAN MCKENZIE (Otology) in the chair. On Thursday the Laryngological Section met and Mr. F. B. GILHESPY read a paper on

Chronic Hyperplasia of the Upper Jaw.

One of his purposes, he said, was to draw attention to the efforts made to include cases of this disease under the wider heading of osteitis fibrosa; another was to indicate some similarities between the condition and that known as otosclerosis. In the eight cases recorded by Westmacott the patients suffered from a bony unilateral enlargement of the upper jaw, and six of them had septic teeth in the affected portion. At the operation the new bone could be gouged away, as it was somewhat soft. The interstices of the bone were occupied by a thick layer of actively proliferating osteoblasts, among them being a few osteoclasts. The vascular supply was rich, and there was an abundance of connective tissue cells. Westmacott's view was that in these cases there was a reversion of the bone to the embryonic type. In none of the eight cases was the premaxilla affected, and this supported the idea that the condition started in the alveolus. In cases of this chronic hyperplasia the cranial bones might be remarkably thickened, so that the inner and outer tables could not be differentiated, the structure of the bone being homogeneous. Mr. G. J. Jenkins had shown that an osteoporotic process might affect the region of the oval window in osteitis deformans, which some regarded as a form of osteitis fibrosa. Mr. Gilhespy asked whether chronic hyperplasia ought to be regarded as a simple fibrous osteitis, or whether it was a localised dystrophy of bone, depending perhaps on a biological variation, and incited to activity by various causes, of which infection from the mouth or teeth might be one.

Mr. WALTER HOWARTH referred to two cases of his own; in one of them he had operated seven years ago, and the condition had remained stationary ever since. The disease had started in the alveolus, and he considered that dental sepsis was the primary cause.—Dr. W. H. KELSON had had two instances of this hyperplasia, neither bearing any relation to oral or dental sepsis. Severe and extensive removal had been found to be unwarrantable.—Mr. RITCHIE RODGER spoke of a case of what was regarded as leontiasis ossium, with large bosses on the left superior maxilla and one on the mandible. The patient disappeared for four years, and then came having several bony rhinoliths. The Wassermann reaction, which previously was negative, had become positive. He suggested this test being done in all such cases as a routine.—Mr. T. B. LAYTON thought there was much evidence of an infective cause of this condition.—Mr. DOUGLAS GUTHRIE showed two slides of specimens of the condition in cases in which there was no dental sepsis.—Mr. JAMES HARPER spoke of three cases under his care. In one a microscopical examination had been made, showing fibrous changes in the bone, but no evidence of malignancy. In one case it would be necessary to remove the jaw in order to save the patient's sight.—Dr. J. S. FRASER said these cases supported his view that otosclerosis was a chronic inflammatory process.—Dr. LOGAN TURNER recommended the appointment of a committee to investigate the subject.

Mr. HOWARTH read a paper on the

Technique of Laryngofissure.

He contended that there were several reasons why tracheotomy should not be done as a preliminary to this operation; for instance, surgical shock was added to by it and blood and secretions were permitted to enter the lungs. Also, direct stimulation of the mucosa did not make for smooth anæsthesia and might facilitate the implantation of cancer cells. He used intratracheal ether for the operation, and did not perform a preliminary tracheotomy. In all these cases the surgeon should be close at hand for 24 hours after the operation. He no longer removed the thyroid ala, though at one time it was his custom. Diathermy was a great help in stopping persistent oozing, but, of course, it could not be used with ether. Diathermy merited careful consideration not only for oozing, but as a means of actually removing the cord.

The PRESIDENT (Dr. WYLIE) said that in two cases in which he did the operation without first performing tracheotomy he had great difficulty on account of hæmorrhage, and tracheotomy had to be done immediately afterwards because the patient coughed so much and he became afraid of pneumonia. Some patients had bronchitis for a time when ether had been used.—Prof. GEORGES PORTMANN (Bordeaux) said that at his clinic at Bordeaux the practice was to do the operation without preliminary tracheotomy, and under local anæsthesia. If, shortly after operation, the patient had respiratory troubles, it was easy to do tracheotomy then.—Dr. SUGARA (Buenos Aires) said that in these cases electrolysis could be used. He did not do tracheotomy first. Great care was taken to stop bleeding at the end of the operation, and electrolysis, very slowly applied, was useful.—Mr. N. S. CARRUTHERS contended that some leakage of blood generally took place, and that this might account for the cases in which there was severe bronchitis.—Sir STCLAIR THOMSON said that Sir Henry Butlin and Sir Felix Semon did not remove the ala of the thyroid, and he himself had at first followed their lead. But he had two or three cases in which some necrosis of cartilage occurred, and portions were coughed up during convalescence. Since he made a practice of removing the ala he had not had any cases of necrosis. On the principle of "safety first," he did preliminary tracheotomy first, especially as it was not dangerous and did not cause shock. The only reliable data were those based upon results in large consecutive series of cases. He had had only three operative deaths—i.e., deaths occurring within a few months of the operation—in his series of 80 cases.—Mr. W. M. MOLLISON spoke favourably of his use of intratracheal ether in two or three cases of laryngofissure. The anæsthetic could be washed out of the patient by the insufflation of air or oxygen at the end of the operation.

Mr. HOWARTH, in reply, said he had had three deaths following laryngofissure—in earlier operation days—chiefly owing to blood entering the trachea. He did not think any leakage could occur during the administration of the anæsthetic.

Mr. LAYTON read a paper on the

Relation of Nasal Polypi to Inflammation of Accessory Sinuses of the Nose.

He said his reason for ventilating this question was that for some time he had been disappointed

with the traditional treatment of nasal polypi by pulling them away. Unless the case were one of a single polypus beneath the middle turbinate he did not find that this method was curative; in other words, for multiple polypi this treatment was no more than palliative. He asked whether polypi ever existed unless there was coexistent disease of a sinus. When there was no sinus disease the polypi were in large airways, and seemed to be in the nature of a hypertrophy to compensate for the extra size of the airway. This type was, he considered, best left alone. In most cases of multiple polypi the underlying disease was an inflammation of accessory sinuses. Nasal polypi might be associated with catarrhal inflammation in the ethmoid and the maxillary sinus. He did not think that acute catarrhal sinusitis ever became acute suppurative sinusitis; his view was that from the beginning they were distinct from each other. When a sinus was the seat of acute suppuration he did not open it. His treatment was to attempt to remove the whole ethmoid by an external incision, so as to avoid damage in the region of the olfactory nerve and the cribriform plate.

Dr. W. S. SYME said he believed that in every case of multiple polypi in the nose there was disease in the antrum as well as in the ethmoid cells. His rule was to open the ethmoid, and he had never regretted having done so.—Mr. C. A. S. RIDOUT thought that the external operation was not done in enough of the cases of multiple polypi of the nose.—Dr. J. S. FRASER said he did not feel that he ought to operate on the antral mucosa for nasal polypi, as in a number of such cases which he had investigated he had found it was healthy. Proof-puncturing and washing out the antrum gave a good indication as to whether it should be operated on. If after clearing the nose the fluid returned at once and freely, obviously the antrum was not filled with polypi. If, however, some force was needed to send the fluid through the syringe, there was obviously obstruction, and the radical operation should be performed.—Dr. SUGARA said that the ethmoid was not implicated in all these cases, because treatment directed to it had no effect in some instances. Radical operation should be carried out when polypi recurred.—Mr. J. ADAM laid stress on the importance of pressure in the causation of polypi. An uvula, if caught between two enlarged tonsils, became polypoid. Polypi would continue to form until the pressure was relieved.—Mr. GILHESPY thought that the external operation could not be done through a small incision; the procedure needed to be thorough, and he always used a longer incision.

Mr. DOUGLAS GUTHRIE read a paper, in collaboration with Mr. N. DOTT, on the occurrence of

Brain-tissue in the Nose,

the so-called nasal glioma. They said that the downward extension of a cerebral tumour towards the nasal cavity seemed to be very rare. They quoted a case of glioma of the frontal lobe of the brain, with an extension into the left nasal cavity.

The patient, a man, aged 33, was admitted because of sudden coma, and symptoms suggesting cerebral compression. There was no history obtainable of any nasal or aural discharge. Following a gun explosion, deafness in the left ear occurred suddenly. Headache, vomiting, and nausea came on later. A week before admission there was sluggish cerebration, and the pulse-rate varied between 54 and 60. The temperature was consistently subnormal. The operation performed was the left subtemporal decompression of Harvey Cushing, and evidences of a deep-lying vascular tumour were found. An attempt was made to expose this. The temperature rose to 105·4° F., and it was very difficult to keep it down. The wound healed soundly, but he died, after a relapse, on the thirteenth day. The tumour, it was found, had been growing backwards and invaded the motor fibres of the internal capsule. There was seen to be a marked convolutional flattening, and a projection at the site of the decompression.

Prof. PORTMANN said it was very difficult to know whether such tumours were simple gliomata or glio-sarcomata.—Dr. FRASER asked whether there was anything distinctive in the appearance of the nose in cases of this kind which could be taken as a warning that something more than ordinary nasal polypus was being dealt with.—Mr. GUTHRIE replied that this patient seemed to have an ordinary polypus, but perhaps the polypus was greyer and harder to the touch than usual.

Mr. M. VLASTO contributed a paper on

Meningitis Originating in the Sphenoidal Sinus.

The sphenoidal sinus, he said, could be regarded as the carrying site of organisms of a non-thrombosing type, usually of low virulence. In the case of meningitis due to infection by other pyogenic organisms, this sinus was a seat of active inflammation. Intracranial complications of sphenoidal sinus suppuration fell into one of the three following groups: (1) meningitis, (2) thrombophlebitis of the venous sinuses, (3) meningitis and thrombophlebitis. Of 42 cases collected by Sir StClair Thomson, 30 died of basal meningitis, and in 17 cases this was the only predominant lesion. He described a typical case, which was reported by Roughton, the patient dying 56 days after admission to hospital. At the autopsy basal meningitis was present, a thick layer of pus being between the region of the optic chiasma and the pons. Mr. Vlasto thought there were many reasons why this condition was not recognised before death. Patients frequently did not realise the gravity of a purulent nasal discharge, and failed to report it. And the diagnosis might be side-tracked by the coexistence of suppurative middle-ear disease. After every death from meningitis, the post-mortem examination should include the opening of the sphenoidal sinus cavities. When an otitic cause of a case of meningitis had been diagnosed and the operative findings were not conclusive, the possibility of sphenoidal sinus infection should be considered.

Dr. P. WATSON-WILLIAMS spoke of the importance of exploring the sinuses in mastoid cases as a routine procedure, even in children.—Dr. LOGAN TURNER urged the need of careful microscopical examination at autopsy, as involvement of the cavernous sinus might be shown.—Sir STCLAIR THOMSON regretted that examination of the sinuses did not seem to be part of the routine post-mortem examination in all hospitals when the lesion was cranial. It could be done without disfiguring the cadaver.

Dr. SYME read a paper in which he gave reports on three bronchoscopic cases, the findings in which prompted him to urge that this form of examination should be done more often.

Progressive Middle-ear Deafness.

On Friday morning the Otological Section listened to a number of papers on this subject.

Dr. G. SCOTT WILLIAMSON and Mr. HORACE RICHARDS read a joint paper in which they submitted a preliminary analysis of a series of cases of chronic deafness, showing lines of possible investigation into the ætiology. Only cases of idiopathic deafness were taken, and all the aspects—cardiac, respiratory, digestive, urinary, neuromuscular, genital, and hæmopoietic—were examined. It was not contended that these tests added materially to the information furnished by the ordinary clinical examination. Fifty-one cases were examined, and seven of these showed signs of established disease. Treatment improved the general condition and with it the tinnitus, which was no longer continuous. The 44 other cases were within the normal, but showed a tendency to tachycardia and their cardio-respiratory balance was easily disturbed. Many facts pointed to the deafness having been started in school life, when there was a low auditory acuity, a real defect in regard to education. In all the 51 cases the nose was small and thin, with a delicate bridge and attenuated skin; the alar muscles were atrophied, and the nostrils no more than slits. But the patients were not mouth-breathers, though they all had nervous instability. There were only five males in

the 51 cases. The physical conditions found seemed to indicate that the deafness was not a mere accident.

Mr. RICHARDS said the deafness complained of had existed for periods of from two to ten years, and its progressive increase was the invariable rule. All the patients except one complained of tinnitus, but evidence as to its duration was unreliable. A history of vertigo was elicited in six cases, of paracusis in five, of recurring colds and catarrh in ten, of recurrent huskiness in five, and of pain, such as earache and headache, in nine. A family history of deafness was forthcoming in only one instance. In several cases there were varying degrees of septal deflection, but without evidence of infection. Marked dental disease was conspicuously absent. Mr. Richards gave a large number of results of hearing and other tests.

Mr. G. J. JENKINS considered that the term "chronic middle-ear deafness" was misleading. The pathology given in most text-books was obviously only speculative, the syndrome seeming to resemble that of an imperfectly described otosclerosis. He had not known middle-ear deafness to be progressive in the sense which was implied by the title of the discussion, which could be attributed only to middle-ear changes.

The PRESIDENT (Dr. MCKENZIE) gave a clinical review of some progressive cases of the condition among his private patients. In 288 cases there was catarrh, in 80 residual cicatrisation, in 136 active suppuration, in 206 otosclerosis, while in 38 there was a combination of three of these conditions. In most of the cases tinnitus was the earliest symptom, having preceded the deafness by months or years. The condition of the membrana tympani gave no indication of the presence or absence of deafness. This type of deafness could not be cured, nor even arrested, by curing the originating catarrh; yet it could be said that the disease process itself was a self-limiting one, as it did not go on to the entire destruction of function. He discussed various possible ætiological factors.

Mr. H. NORMAN BARNETT considered that progressive middle-ear deafness could be divided into (1) that following long antecedent middle-ear suppuration, or secondary to tonsil infection or septal deflection, and (2) that in which these factors were absent but in which there had been infection through the Eustachian tube, or other trouble. His treatment was directed to causing absorption of the deposited material and the breaking down of adhesions by oto-massage of the tympanic membrane, ionisation over the mastoid, and the passage of various vapours into the middle ear. He showed three successful cases.—Dr. FRASER thought that the best classification of these cases was into those with normal tympanic membranes, and those with abnormal tympanic membranes. In his experience, chronic catarrhal otitis media was now a diminishing quantity, whereas otosclerosis was on the increase.—Sir JAMES DUNDAS-GRANT believed that many cases of chronic progressive middle-ear trouble were secondary to a narrowing of the walls of the Eustachian tube. A negative Rinné might be due to unilateral nerve deafness.

Mr. SOMERVILLE HASTINGS dealt with auditory intelligence, which had much to do with the apparent hearing acuity as tested by the audiometer. He believed that otosclerosis properly so-called was very rare. He thought the right course was to search carefully for sepsis in every case, and treat it. A good result might not ensue in every case, but it would occur in a sufficient proportion to make it worth while.

Mr. J. F. O'MALLEY said that in some of these cases there was evidently a hereditary factor—namely, a definite middle-ear catarrhal trouble which led to deafness. During a cold there was definite deafness, but on losing the cold the hearing was restored. If hearing did not clear up, an otosclerotic change took place in the labyrinth. He thought otosclerosis was becoming more frequent.

The discussion was continued.

Dr. GRAHAM HODGSON demonstrated a large series of radiograms of the normal and abnormal labyrinth, and Mr. WATKYN THOMAS gave a clinical description of the cases illustrated.

Cinematograph Demonstration.

On Saturday morning, before the discussion of clinical cases, Prof. PORTMANN gave a cinematograph demonstration of an operation for draining the saccus endolymphaticus for the relief of vertigo. He began his dissertation by discussing the comparative anatomy of the auditory apparatus of various orders and species, leading up to that of man. He then passed to a consideration of the physiology and function of the saccus endolymphaticus and minutely described the surgical entry to that structure for the purpose of incising and draining it for the relief of vertigo. In two of his five cases there had been a complete disappearance of the vertigo. The operation, he declared, was a good one and was not dangerous in the hands of an otologist. It was intended for cases in which other forms of treatment had failed to relieve the vertigo.

Dr. JOBSON HORNE gave an epidiascopic demonstration of morbid specimens of the saccus endolymphaticus, showing the course of the disease, and the results which ensued in a number of cases. He said this structure might be regarded as an instance of how the vestigial remains of an embryonal structure might become a source of danger.

Sir CHARLES BALLANCE expressed the thanks of the Section to Prof. Portmann for his admirable demonstration, and said that perhaps operation in the way indicated might be tried in some cases of deafness as well as for vertigo.

A discussion followed.

BRIGHTON AND SUSSEX MEDICO-CHIRURGICAL SOCIETY.

AT a meeting of this Society held on June 2nd, Dr. E. RIVAZ HUNT, the President, in the chair, Dr. E. R. FOTHERGILL opened a discussion on

Mental Exhaustion and Drug Addiction.

To the sufferer from mental exhaustion, he said, the advice of friends is generally worse than useless, and until the patient settles down to deal with his trouble, and stops thrusting it back into the subconscious, all else will fail. The first step to be taken is to secure an appropriate atmosphere and the services of an attendant. The patient should go to bed, and after constipation—from which these patients usually suffer—has been dealt with, he should be given full diet. He should be encouraged to get his brain to sleep until the physical state has been re-established, by which time many of the symptoms will have disappeared. It will then be time enough to discover from the patient the cause of his illness, and to treat it. As much sleep as possible should be obtained. At first no books or papers should be allowed, but after a while the patient will probably ask to see a picture paper. The date on which this happens should be noted. The relatives should not have any communication with the patient, except by an occasional postcard, but the doctor should be assisted by them to discover the possible cause of the illness. Records of weight should be taken at intervals of 14 days. The patient must first be got to believe that there is no physical or mental disease and that his trouble can be dealt with; he must cease deploring the past and dreading a repetition of it, and must be encouraged to turn his thoughts to the future into a constructive channel. Relatives either regard the question of certification with horror, or find it attractive because of ulterior motives. Great care must be exercised. There are

many people of undoubtedly unsound mind who can be brought back within a very short while if suitably treated. Should certification be delayed on this account, it is as well to secure the support of another doctor for the delay, and to place the facts before the Board of Control.

Two facts that stood out in his experience of drug addiction, said Dr. Fothergill, were that, apart from alcoholism, it is found only amongst intellectuals, and that without corroborative evidence nothing the patients say is to be relied on. A voluntary addict, without disease or injury as the excuse, must be regarded as having been potentially mentally unbalanced. If this is accepted, then treatment will follow on similar lines to that for mental exhaustion, as it would be useless to treat the drug addiction without treating the underlying cause. Drug addiction as the result of disease or injury becomes increasingly difficult to treat when the physical reasons for giving the drug are gone. Where there is no disease or injury, the treatment is by tapering—in the case of alcohol, at the commencement; with morphia and its derivatives, at the end. It must be certain that no drugs can reach the patient without knowledge of the attendant or the doctor. The amount of liquid in the barrel of the syringe, or the size of the suppository, must never be varied. As the treatment progresses, and the strength of the dose is decreased, it must be anticipated that the patient will become more difficult to handle.

Reviews and Notices of Books.

SECRETION OF THE URINE.

Second edition. By A. R. CUSHNY, M.A., M.D., LL.D., F.R.S., late Professor of Materia Medica and Pharmacology in the University of Edinburgh. London: Longmans, Green and Co., Ltd. 1926. Pp. 283. 16s.

ONLY those who have worked on the problem of urinary secretion are in a position adequately to assess their debt to the author of this monograph. The first edition, which appeared in 1917, proved a monumental landmark, for before its advent the masses of uncorrelated facts had merely led to a chaos of hypothesis and misrepresentation. The value of a scientific theory is not to be reckoned entirely by its power to explain the experimental facts elicited in the past, but also by the extent to which it can be readily modified in order to bring it into line with the latest established facts. Cushny's theory of the mechanism of the secretion of urine illustrates these desirable qualities to a high degree.

In this edition further evidence in favour of filtration as being the function of the glomeruli is included, emphasis being laid on the experiments of Weam and Richards in the frog and on those of Starling and Verney, who used the heart-lung-kidney preparation in the dog. Cushny originally imputed to the tubules the simple function of reabsorbing a fluid of unvarying composition from the glomerular filtrate, this fluid being an optimal fluid and presumably resembling Locke's fluid in its composition. The theory of reabsorption by the tubule cells has been strengthened by recent work both in the case of the frog and in that of the mammal, but the original conception by the author of the simplicity of composition of the fluid reabsorbed is no longer in accordance with the experimental facts. A comparison of the concentration ratios of, for example, urea and sulphate in plasma and urine shows that that of sulphate is higher than that of urea. Urea therefore cannot be regarded as a no-threshold substance. Such observations necessitate a change in our conception of the nature of the reabsorbed fluid, so that we now look upon this fluid as containing the following substances: water and glucose; chloride and bicarbonate; potassium, urea, and urate; phosphate; sulphate, creatinin, and foreign substances—the degree to which each of these substances is reabsorbed varying inversely with its position in the group; that is to say, water and glucose show the highest degree of reabsorption, creatinin the lowest.

The "modern theory of urinary secretion," originally outlined by Cushny, has thus been slightly modified to conform to the facts elicited by recent researches. In its present form it retains the valuable qualities of simplicity of conception and of incentive to further work and can best be studied in the monograph prepared by Prof. Cushny before his death.

SEMILUNAR CARTILAGES OF THE KNEE.

Pathologie des Ménisques du Genou. Par ALBERT MOUCHET, Chirurgien des Hôpitaux de Paris; et LOUIS TAVERNIER, Professeur agrégé à la Faculté de Médecine de Lyon, Chirurgien des Hôpitaux. Paris: Masson et Cie. 1927. Pp. 98. Fr.18.

THIS monograph embodies the report on the subject presented by the authors to the thirty-fifth French Congress of Surgery, which met at Paris in 1926. Internal derangement of the knee-joint has for many years been a familiar subject of discussion in this country, and later in America, but in France it has attracted little attention till recently; possibly the vogue of football in that country has drawn attention to it, although, as is well known, such injuries as displacement of a knee cartilage are common among miners in all countries.

After shortly describing the normal anatomy of the parts concerned, the authors turn to pathological anatomy and describe the lesions which most generally are found after injury. As to traumatic meniscitis, described by Roux, of Lausanne, the authors conclude that it is not a pathological reality, and that the changes found do not concern the fibrocartilages themselves. They hold the view that rotation of a flexed knee is not necessarily one of the causes of damage to the cartilages, for they have recorded cases in which simple forcible extension without rotation has produced rupture of a meniscus. The determining cause, in their opinion, is some interference with free movement between condyle and fibrocartilage. Among secondary complications they mention loose bodies, dry arthritis, and injury to ligaments. They are agreed with previous observers as to the preponderating frequency of injuries of the internal cartilage. After considering the claims of Roux to have cured "meniscitis" by massage, the authors dispute, as aforesaid, the existence of this lesion, and hold that Roux's cases were really those of limited tearing of a cartilage, which cannot be cured by massage. Meniscopexy or fixation of the torn cartilage is dismissed in a few words as useless. The operation of arthrotomy for removal of torn cartilages, which the authors favour, is one by a transverse incision which no doubt gives a better view of the interior of the joint than does a longitudinal one, but which, as described by them, involves division of one of the lateral ligaments of the joint. The importance of early active movements after operation, in order to prevent stiffness, is properly emphasised. Proper caution is advocated in cases in which the symptoms are equivocal; many of these clear up without arthrotomy, showing no rupture of a cartilage.

The last few pages are devoted to consideration of cysts of the cartilages. Such cysts are almost entirely confined to the external cartilage. Excision of the cartilage and cyst is the only proper treatment. The book is well illustrated with 26 figures, most of which are semidiagrammatic drawings, which are better than photographs for their purpose. It should be of value in France, where monographs on the subject are rare, but in this country, where so much has been done and written in the surgery of the knee-joint, it is less likely to attract attention.

TREATMENT OF DIABETES MELLITUS.

Fourth edition. By O. LEYTON, M.D., F.R.C.P., Physician to the London Hospital. London: Adlard and Son, Ltd. 1927. Pp. 98. 6s.

THE discovery of insulin and the revolution which it has worked in the treatment of diabetes has necessitated a new edition of Dr. Leyton's book and caused a change of its name from "The Modern (Allen) Treatment of Diabetes Mellitus." The new edition has been largely rewritten and is now a plain statement of Dr. Leyton's views and practice, set out in simple language. A glossary of medical terms is included so that patients may read and understand. In the preface is a statement of some importance showing clearly the ideals on which the author works. He says: "One has reason to believe that the beta cells of the islets of Langerhans regenerate in time, but the process is a slow one, and the recovery may take years to become complete. This chance of recovery makes it advisable for all patients except those in extreme old age to arrange a diet which suffices to nourish their bodies and sufficient insulin to keep the blood-sugar below 0·15 per cent., and thereby avoid over-stimulation of the newly formed insulin-producing cell, which would lead to its early destruction." The importance of care in making the diagnosis is emphasised and the condition of renal glycosuria or, as Dr. Leyton prefers to call it, negligible glycosuria, is explained very carefully. The test for sugar tolerance by giving the dextrose intravenously seems rather complicated and the alternative method of allowing the patient to eat an ordinary diet for six months before repeating the test a little risky. Many clinicians would prefer to restrict the diet to a certain extent and repeat the test in three months or sooner. The diet scheme remains unaltered and still starts with a period of fasting which may last for four days on occasion. If sugar is still present, insulin is then started. The subsequent stages of the diet are designed to increase the carbohydrate value daily until the diet, on the fifteenth day, contains 49 g. of carbohydrate, 52 g. of protein, and 117 g. of fat; caloric value 1460. If this amount of food satisfies and the blood-sugar is normal no insulin is given and the diet is kept at this level for many months. Dr. Leyton does not mention the alternative method of treatment with a maintenance diet of about the same value as that of his fifteenth day. There are two schools in England, just as there are in the United States, and Dr. Leyton belongs to the one which believes that a short period of under-nutrition increases the chance of recovery of sugar tolerance much more than the alternative method. He also never uses the high carbohydrate and high insulin treatment advocated by some writers. The rules for the administration of insulin are clearly set out. A knowledge of the blood-sugar is very important, and as it is often difficult for patients who live away from laboratories to have this estimated, Dr. Leyton is accustomed to teach patients how to do this by Folin and Wu's method. The index is adequate. The food tables are sufficiently detailed for most patients.

RECENT ADVANCES IN HÆMATOLOGY.

By A. PINEY, M.D., Research Pathologist, London Cancer Hospital. London: J. and A. Churchill. 1927. Pp. 272. 12s. 6d.

IN his introduction the author describes hæmatology as "that branch of biological science which deals with the morphology of the blood and blood-forming tissues." Hæmatology as thus defined is a subject of which it is difficult to describe the recent advances, on account of their extreme paucity. Almost the only section of the volume containing matter that falls strictly under this head is that concerning the hæmorrhagic diatheses. In the knowledge, and to a less extent in the treatment of these conditions, notable advances have been made in the past few years, and these are adequately summarised by Dr. Piney. This is the first volume to appear in this country in which a serious attempt has been made to bring together the recently won knowledge on the subject. It is a matter for regret that considerations of space did not permit an even more extensive excursion into this field. The one other direction in which notable advance has been made in the knowledge of the blood, that of the blood groups and their significance, has not been regarded by the author as coming within the scope of the work. A section on this subject would, however, have greatly enhanced its value. For the rest this volume follows in a competent manner the usual lines of text-books on the morphology of the formed elements of the blood and of the blood-forming tissues, and is a useful and complete compendium of the present state of knowledge on this subject.

PATHOLOGICAL MICRO-ORGANISMS OF THE EYE.

Die pathogenen Mikro-organismen des Auges. By Prof. Dr. F. v. HERRENSCHWAND. Berlin and Vienna: Urban and Schwarzenberg. 1927. With 17 illustrations and 12 coloured plates. Pp. 310. M.24

Dr. Axenfeld's work on the Bacteriology of the Eye came out in 1908, and was at once translated into English by Angus McNab, one of the early victims of the war. Prof. Herrenschwand does not desire to compete with that work, but to provide one which shall prove supplementary to it and to bring the subject up to date. The scheme of his book differs somewhat from that of Axenfeld's. After an introductory chapter on the general morphology of pathogenic bacteria, each organism pathogenic to the eye is dealt with fully, including its relation to other pathological conditions both of men and of animals; the results of injections of the organism into animals are described, and the diseases of the eye which it is liable to cause in man are stated. A bibliography of the literature bearing on each micro-organism in turn is appended, and since this is brought up to the end of 1926, it should prove especially valuable. If we may select one section of the book as of peculiar importance it is that dealing with the recent work on *Spirochæta pallida*. In an appendix directions are given for the collection of material from the eye, and for methods of staining, cultivation, and inoculation. The 12 coloured plates, each with from four to seven reproductions of drawings from stained specimens, leave nothing to be desired.

The work will be valued in every library attached to a pathological ophthalmic department.

MIND AND PERSONALITY.

By WILLIAM BROWN, M.D., M.R.C.P., D.Sc., Wilde Reader in Mental Philosophy, Oxford. London: University of London Press. 1926. Pp. 354. 12s. 6d.

Dr. Brown's readable volume can only be treated with justice if it is regarded as a collection of essays rather than a work with a unified thesis. That the author has a point of view we have little doubt. But it is due to a philosophic attitude rather than a scientific detachment which finds a thesis from the examination of data of experience. Philosophy rather than psychology seems to be the author's pursuit. He appears to be bothered by the universe rather than curious about it. In scanning a wide cultural horizon for some philosophic resting-place he pauses from time to time to quarry in the strata of the human mind, but his researches are always metaphysically coloured. This by no means detracts from the interest of the volume before us. It gives everything with which he deals a background against which empirical data derived from experimental psychology and clinical psychology are thrown into relief and acquire a value and a meaning which, if a little alien to the detached method of science, will prove satisfying and restful to those of us who, immersed in the welter of discrete facts, find solace in the unifying value of philosophy. Philo-

sophically Dr. Brown is deeply indebted to Bergson—a philosopher who in many ways has done as much for the affective life in philosophy as Freud has done for it in psychology. There are essays of course dealing with subjects of practical psychological significance, and some of them form excellent epitomes of recent work in particular fields. For example, the chapter on Mind and Experimental Methods will be to the beginner a very valuable survey of the introduction of laboratory methods into psychology, and here the author speaks as one in authority. The chapter on Mathematical Ability is equally good. Dr. Brown gives us of his experiences in the psychopathological field, and while distinctly impressed by the psycho-analytic approach is by no means carried away. He is to be congratulated on having been deeply analysed without suffering a scorch mark in the passage through the fire—he found his religious attitude remained unchanged. In our experience this is rare.

Dr. Brown's volume will be a stimulus to those who are not actually engaged in psychopathology and a pleasant interlude to the specialist who needs a little philosophic leaven added to his occasionally arid researches.

MEDICAL DIATHERMY.

Leitfaden der Diathermiebehandlung. By A. LAQUEUR, Medical Director of the Hydrotherapeutic and Mechanotherapeutic Institute of the Rudolf Virchow Hospital, Berlin. Berlin: S. Karger. 1926. Pp. 134. M.4.80.

Die Klinische Anwendung der Diathermie. By Dr. IWAN VON BÜBEN, Assistant in the Frauenklinik of the University of Budapest. With a foreword by Prof. Dr. BELA V. KELEN, Director of the Röntgen Institute of the University of Budapest. Leipzig: Johann Ambrosius Barth. 1926. With 85 illustrations. Pp. 175. M.11.40.

Anleitung zur Diathermiebehandlung. Second edition. By Dr. G. BUCKY. Berlin: Urban and Schwarzenberg. 1927. With 132 illustrations. Pp. 200. M.6.

A GOOD impression of the extent of the therapeutic field of medical diathermy and the progress that has been made by German and Austrian specialists in the subject is conveyed by three books published in Berlin and Leipzig during the last year. In all of them brief introductory accounts are given of high-frequency currents and the relevant physical principles. The path and distribution of these currents in various conductors and methods of applying them to different regions of the body are described. The action of the diathermy current on the body in health and in disease is shown, and the subject of dosage is considered. The maladies which respond to diathermy and methods of applying the treatment are discussed under the headings of the different systems and regions of the body, surgical diathermy being less fully considered than medical diathermy. Dr. von Büben devotes only 22 pages to it, while the other authors give mere introductory outlines.

Dr. von Büben speaks highly of the value of diathermy in gynæcology, particularly in cases of chronic infection of the uterus and urethra and of the pelvic supporting tissues. In the treatment of sciatica he describes a method in which three electrodes are applied respectively to the back of the hip, front of the thigh just above the knee, and to the middle of the leg. These electrodes are connected to the three terminals of the diathermy machine. He seems to think that better results are obtained when the whole length of the nerve is subjected to diathermy than when the treatment is applied to the regions to which the pain is referred. Dr. von Büben's book is clearly printed in large type and has a number of useful illustrations.

Dr. Laqueur's book, smaller in size and with fewer pictures, will be a useful guide to those who wish to learn the essentials of the subject. The author describes some interesting experiments which he conducted in order to show the influence of diathermy on organisms introduced into the knee-joints of dogs. He showed that organisms such as the cholera vibrio, the pneumococcus, and the gonococcus, which are sensitive to moderate degrees of heat, were either destroyed or rendered much less virulent after diathermy had been applied to the joints, while the temperature reached did not damage the tissues of the host.

Dr. Bucky's book is an enlarged edition of a work written as long ago as 1911; it contains a number of useful line drawings which show the position of the electrodes for the treatment of different regions. Under the headings of various diseases the author describes, in tabular form, the method of action of the diathermy, the course of the disease and the results of the treatment, the method of application of the current, and the frequency. Of special interest is the so-called "alternator" devised by Dr. Bucky himself. By its means the operator is able to direct the current through regions by the "cross-fire" method. In this way a greater degree of heat may be obtained in deep regions without undue heating of the superficial tissues. Dr. Bucky also describes his "pulsator." By means of this instrument the current is made to oscillate intermittently. The author believes that better results can sometimes be obtained when this instrument is used. Dr. Bucky calls attention to a curious and uncommon form of burn which may be caused in the subcutaneous fat when the diathermy current is passed through the skin and superficial fascia. Fat offers a much higher resistance to the current than the skin and can be damaged by a diathermy current which is insufficient to harm the skin.

The books by Bucky and von Büben contain, in index form, abundant references to the literature of medical diathermy.

SCIENCE AND RELIGION.

The Creator Spirit. By C. E. RAVEN, D.D., Canon of Liverpool. London: Hopkinson and Co. 1927. Pp. 310. 8*s.* 6*d.*

THERE have been a number of books and papers lately about science and religion. This one strikes us as one of the best and most helpful, especially for those who are not very deeply trained in technical philosophy. It is based on Hulsean lectures given in Cambridge, England, and Noble lectures in Cambridge, Mass., and Canon Raven brings into the discussion a range of knowledge in history, theology, philosophy, and biology which is an admirable equipment for his active churchmanship. He adds, too, the special qualification of being a good field naturalist, and draws many illustrations from his personal knowledge of birds and moths—a line of study which brings out clearly the problems which biology has to solve if it does not do very much to solve them. Broadly speaking, the author is an emergent evolutionist who rejects altogether the probability of any dualistic interpretation of human experience. Religion is an imperfect explanation in so far as it fails to explain the fields which have been specially explored by naturalists; the scientific account of the world fails by as much as it excludes religious data. Evolution has proceeded in one continuous series from the electron, through atoms, molecules, substances, life, intelligence, spirit, to the saint which is the culmination that we can at present apprehend; it has happened neither by luck nor cunning but by the love of God. Canon Raven assumes as axiomatic what is fundamental to the Christian position; he states the case against Darwinism too emphatically; the discussion comes, as it seemingly must always come, to points which are self-evident to one mind and incomprehensible to another. But the whole is a sincere and able attempt to achieve progress in a line where progress at last seems possible, and where it would be welcomed by at least as many naturalists as theologians. We commend it heartily.